

# FIG. 1A

pET22b(+) forward primer:

5'-CGGGATCCT TCT GTT GAT CAC GGC TTC-3' (SEQ ID NO:3)

pET22b(+) reverse primer:

5'-CCCAAGCTT TGT TCT TCT CAT ACA GAC-3' (SEQ ID NO:4)

pPICZ $\alpha$ A forward primer:

5'-TTCGGAATT C TCT GTT GAT CAC GGC TTC-3' (SEQ ID NO:15)

pPICZ $\alpha$ A reverse primer:

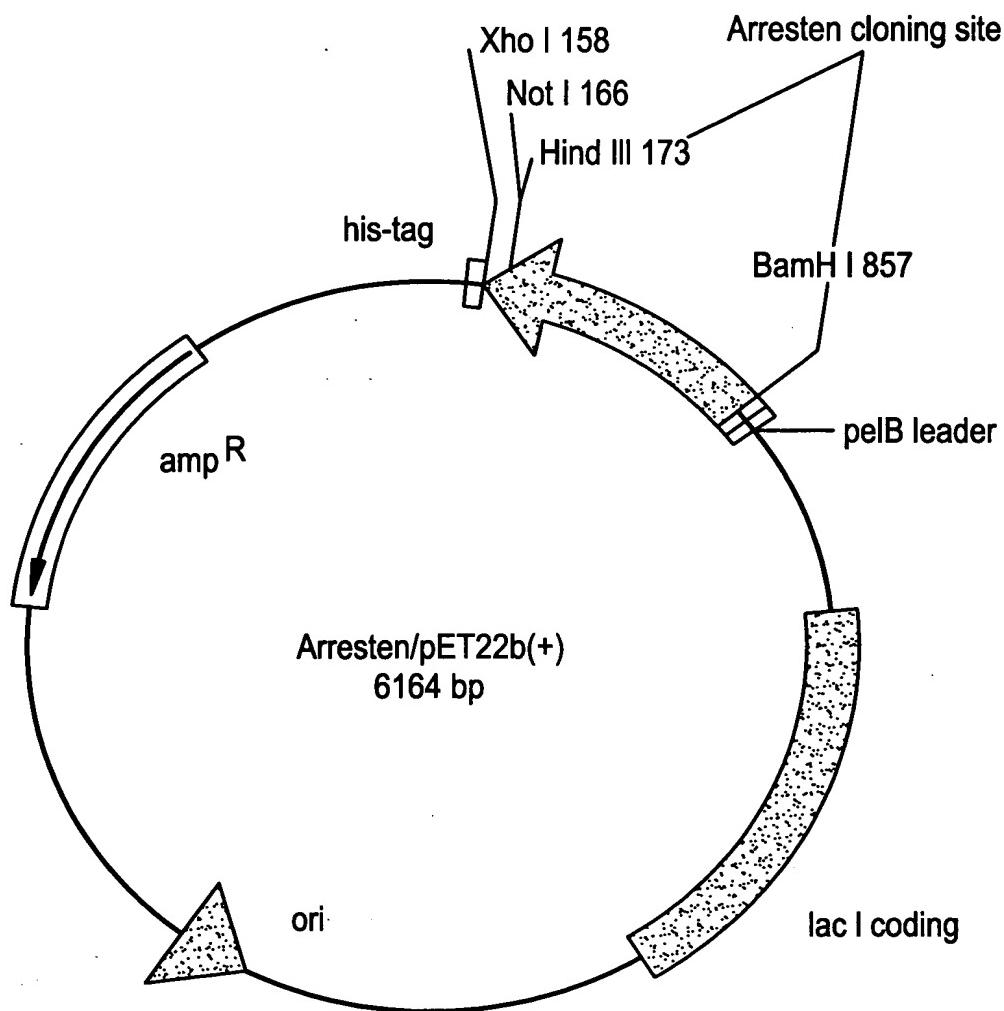
5'-TGCTCTAGAGG TGT TCT TCT CAT ACA GAC TTG GCA-3' (SEQ ID NO:16)

5	10	15	20	25	30	35	40	45
tct	qtt	qat	cac	qqc	ttc	ctt	gtg	acc
50	55	60	65	70	75	80	85	90
gat	gac	cca	cag	tgt	cct	tct	ggg	acc
95	100	105	110	115	120	125	130	135
tac	tct	ttg	ctc	tac	gtg	caa	ggc	aat
140	145	150	155	160	165	170	175	180
gac	ttg	ggc	acg	gcc	ggc	agc	tgc	aca
185	190	195	200	205	210	215	220	225
ccc	ttc	ctg	ttc	tgc	aat	att	aac	aac
230	235	240	245	250	255	260	265	270
cga	aat	gac	tac	tcg	tac	tgg	ctg	tcc
275	280	285	290	295	300	305	310	315
atg	tca	atg	gca	ccc	atc	acg	ggg	gaa
320	325	330	335	340	345	350	355	360
agt	agg	tgt	gct	gtg	tgt	gag	gcg	cct
365	370	375	380	385	390	395	400	405
cac	agc	cag	acc	att	cag	atc	cca	ccg
410	415	420	425	430	435	440	445	450
tcg	ctg	tgg	atc	ggc	tac	tct	ttt	gtg
455	460	465	470	475	480	485	490	495
gca	gaa	ggc	tct	ggc	caa	gcc	ctg	gag
500	505	510	515	520	525	530	535	540
gag	gag	ttt	aga	agt	gcg	cca	ttc	atc
545	550	555	560	565	570	575	580	585
acc	tgc	aat	tac	tac	gca	aac	gct	tac
590	595	600	605	610	615	620	625	630
ata	gag	agg	agc	gag	atg	ttc	aag	aag
635	640	645	650	655	660	665	670	675
aag	gca	ggg	gag	ctg	cgc	acg	cac	gtc
680	685	690						
atq	aga	aga	aca	taa				

(SEQ ID NO:1)

## FIG. 1B

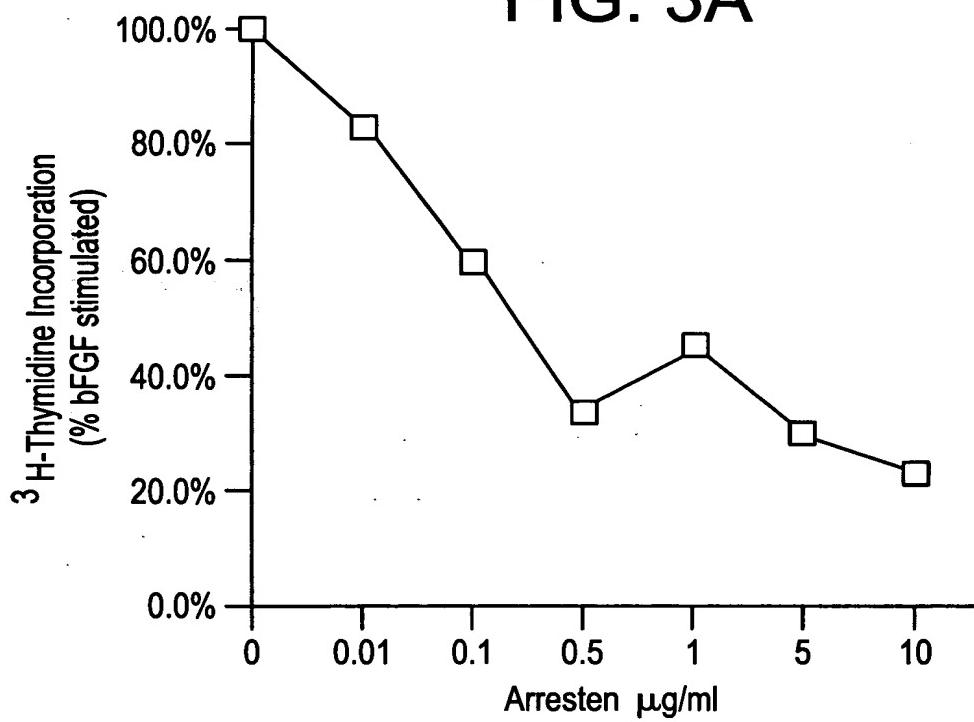
5 10 15 20 25 30 35 40 45  
SVD HGF LVT RHS QTI DDP QCP SGT KIL YHG YSL LYV QGN ERA HGQ  
50 55 60 65 70 75 80 85 90  
DLG TAG SCL RKF STM PFL FCN INN VCN FAS RND YSY WLS TPE PMP  
95 100 105 110 115 120 125 130 135  
MSM API TGE NIR PFI SRC AVC EAP AMV MAV HSQ TIQ IPP CPS GWS  
140 145 150 155 160 165 170 175 180  
SLW IGY SFV MHT SAG AEG SGQ ALA SPG SCL EEF RSA PFI ECH GRG  
185 190 195 200 205 210 215 220 225  
TCN YYA NAY SFW LAT IER SEM FKK PTP STL KAG ELR THV SRC QVC  
229  
MRR T (SEQ ID NO:2)

**FIG. 2**

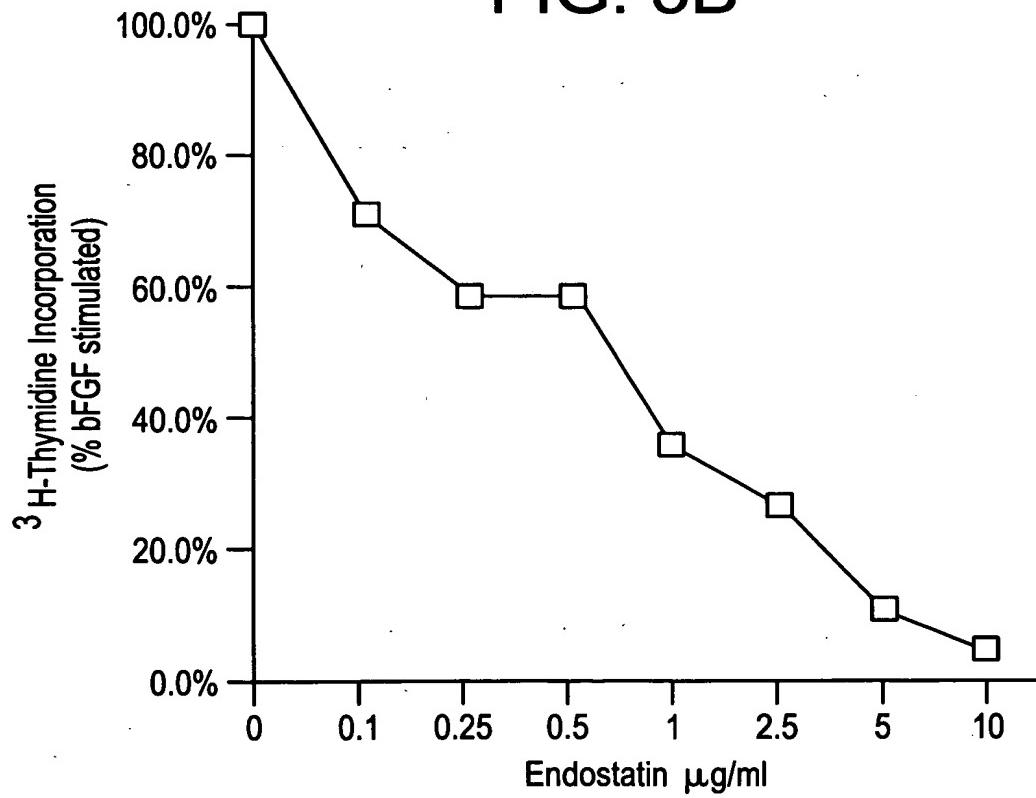
Forward primer: 5'-cgggatccctctgttgtacacggcttc-3'

Reverse primer: 5'-cccaagcttgcgtttcatacagac-3'

**FIG. 3A**



**FIG. 3B**



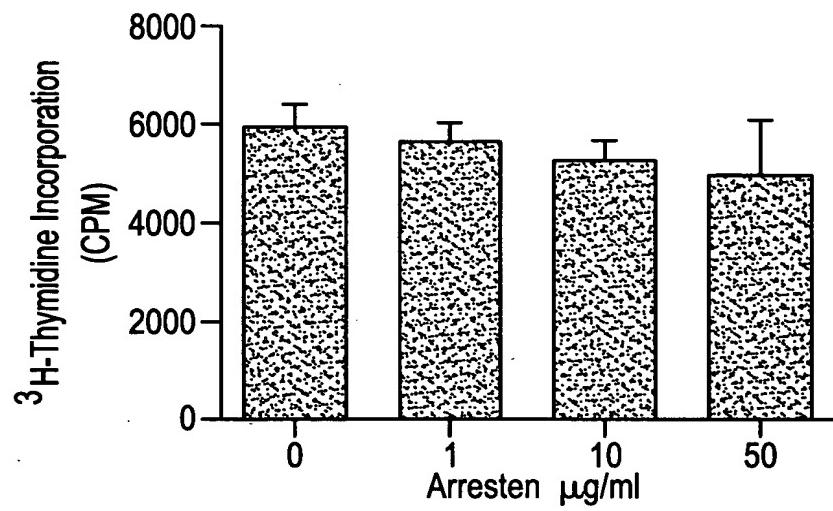
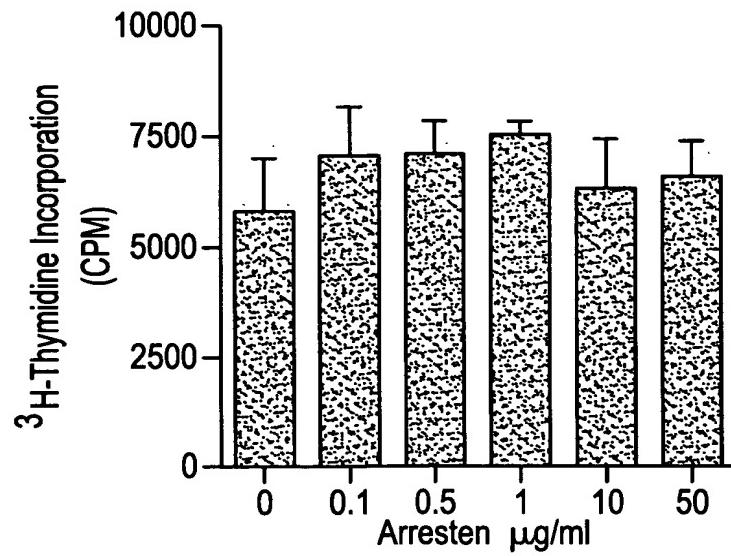
**FIG. 4A****FIG. 4B**

FIG. 4C

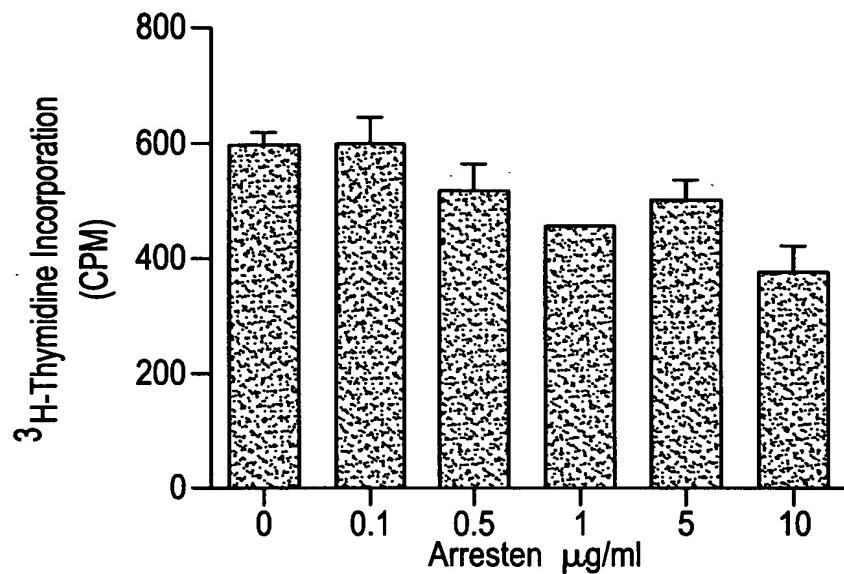
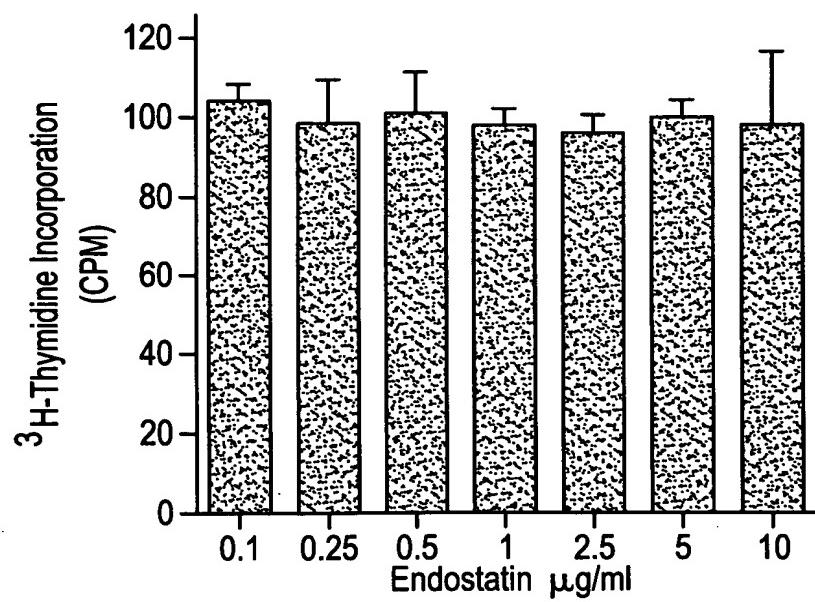


FIG. 4D



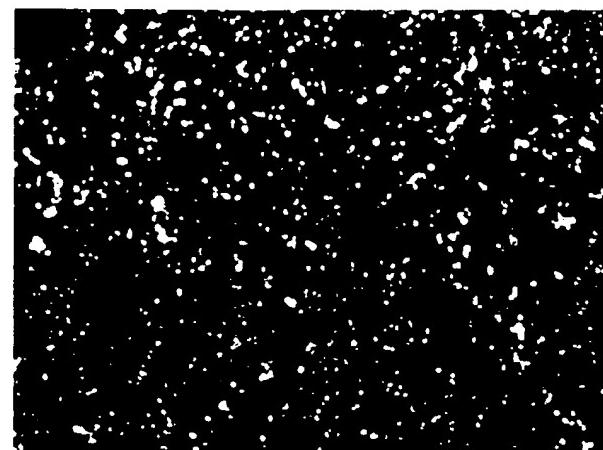
Docket No.: 1440.1027-016

Title: ANTI-ANGIOGENIC PROTEIN AND...

Inventors: Raghuram Kalluri

## FIG. 5A

Control



## FIG. 5B

Arresten 2 µg/ml



## FIG. 5C

Endostatin 20 µg/ml



FIG. 6

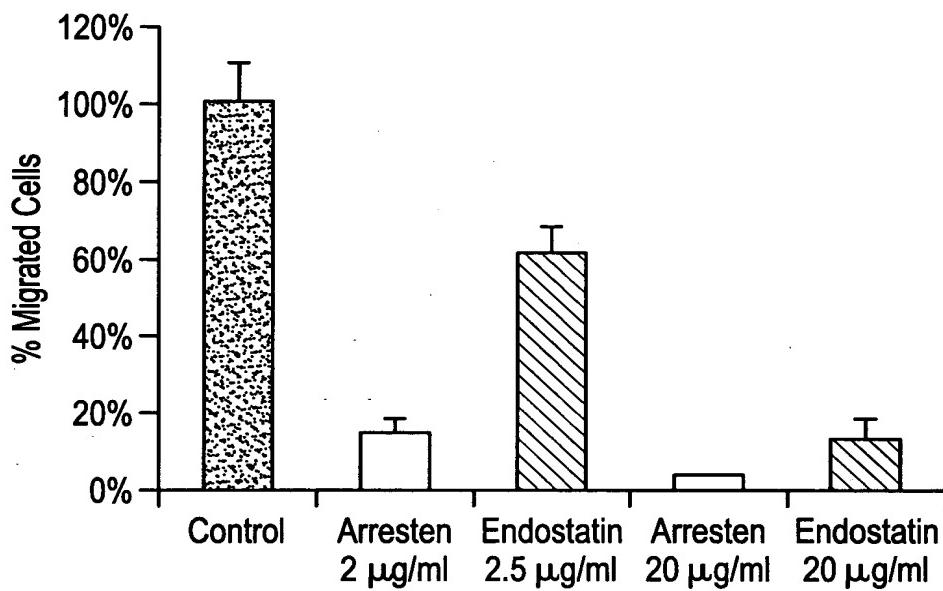
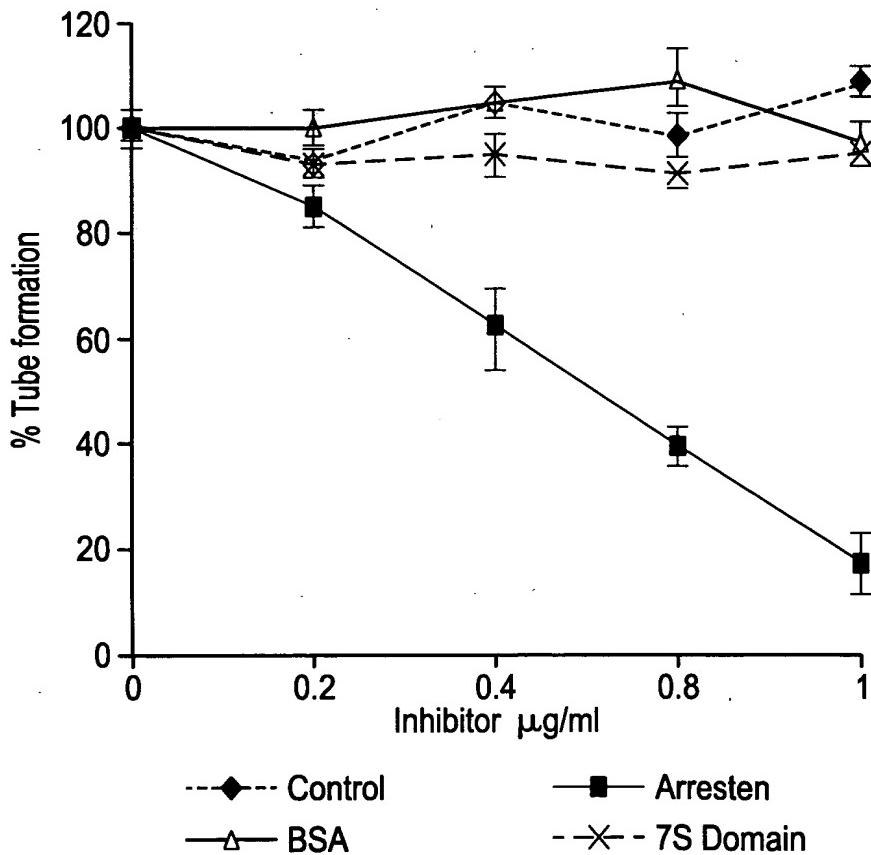
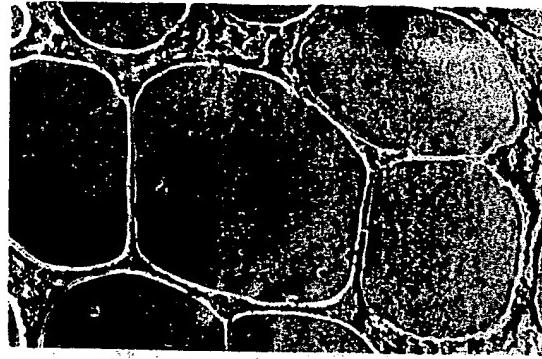


FIG. 7



**FIG. 8A**



**FIG. 8B**



FIG. 9A

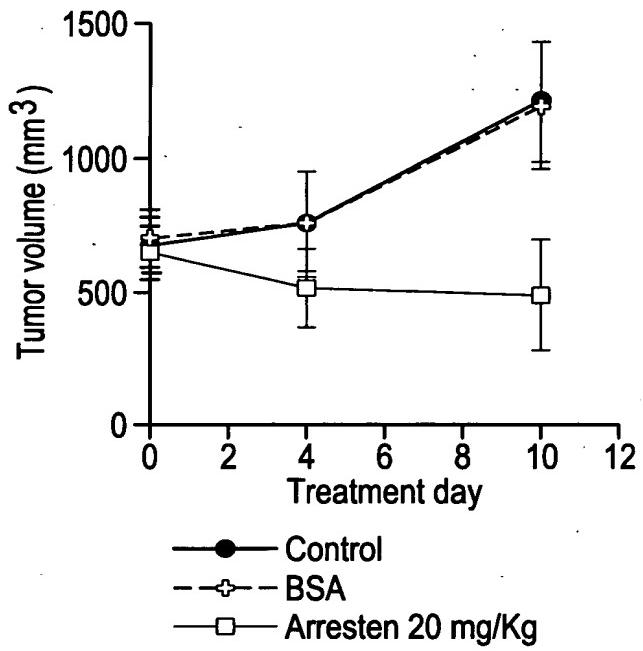


FIG. 9B

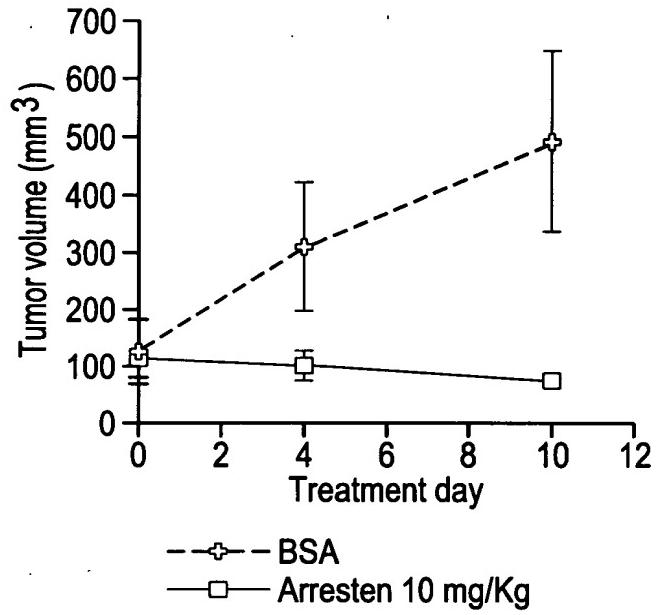


FIG. 9C

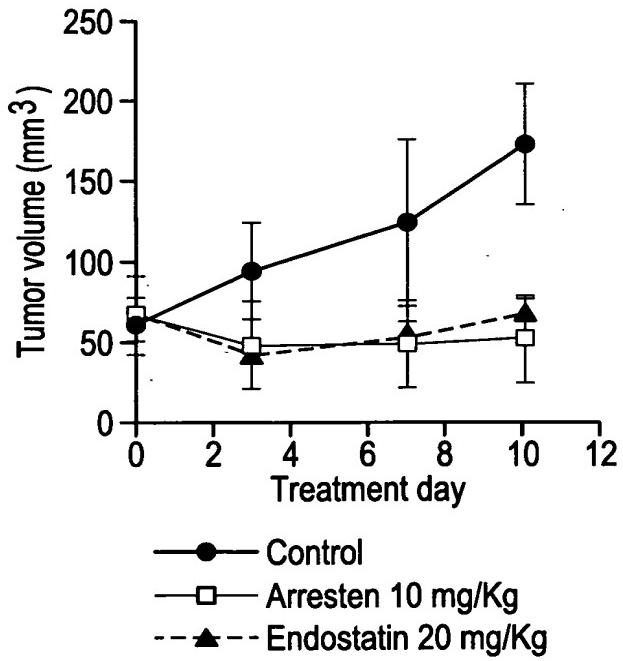
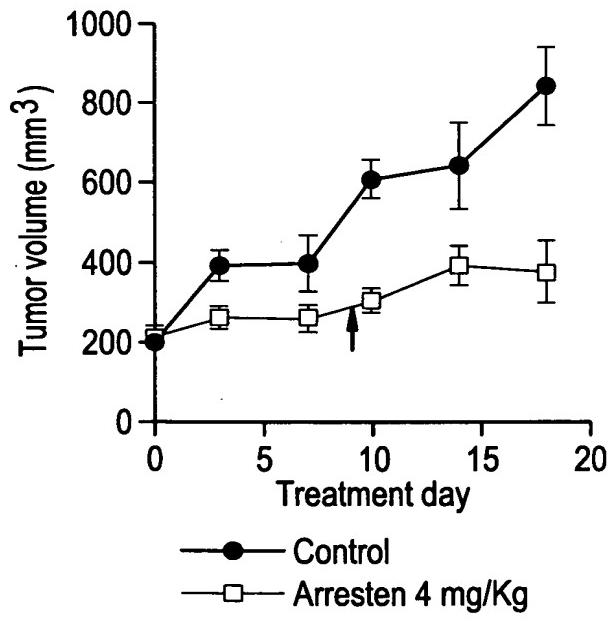
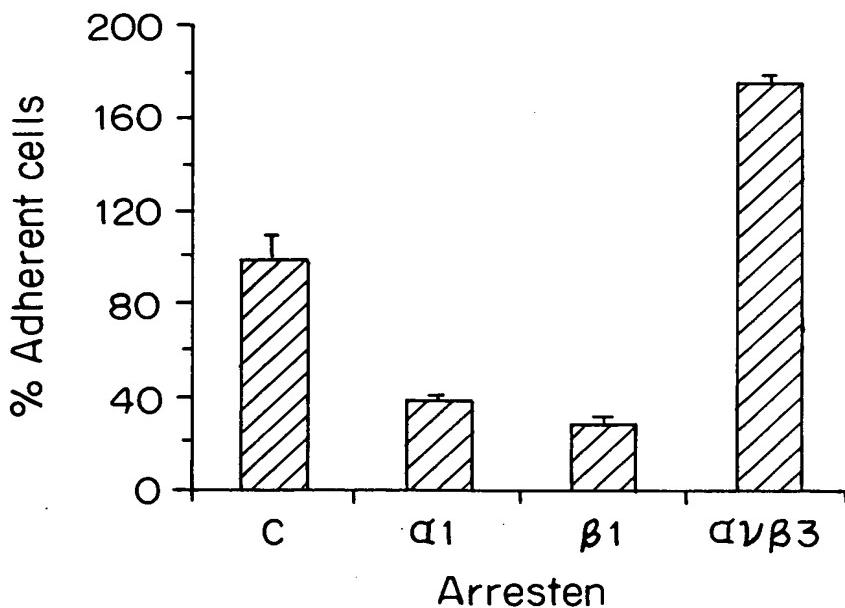
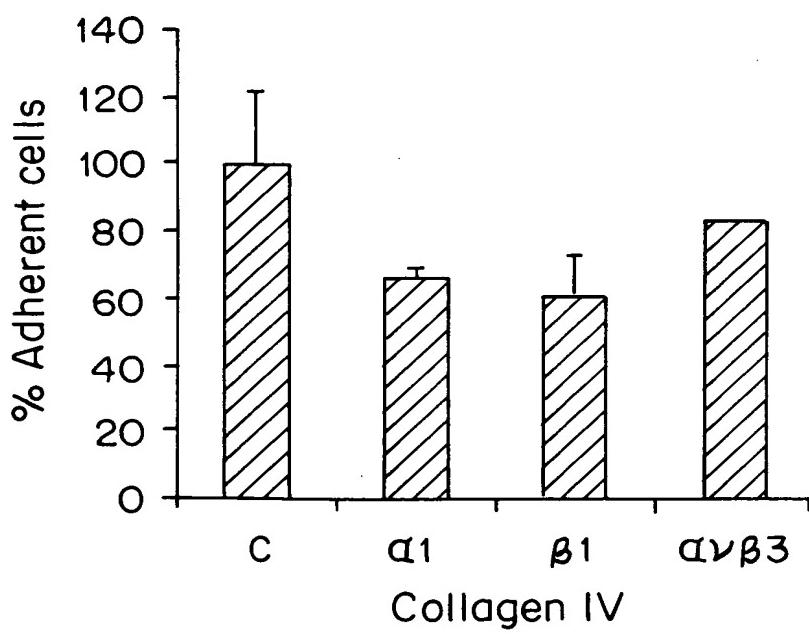


FIG. 9D





**FIG. IOA**



**FIG. IOB**

## FIG. 11A

pET22b(+) forward primer:

5'-CGGGATCCT GTC AGC ATC GGC TAC CTC-3' (SEQ ID NO:7)

pET22b(+) reverse primer:

5'-CCCAAGCTT CAG GTT CTT CAT GCA CAC-3' (SEQ ID NO:8)

pPICZ $\alpha$ A forward primer:

5'-TTCGGAATTC GTC AGC ATC GGC TAC CTC CTG-3' (SEQ ID NO:17)

pPICZ $\alpha$ A reverse primer:

5'-GGGGTACCCC CAG GTT CTT CAT GCA CAC CTG G-3' (SEQ ID NO:18)

5	10	15	20	25	30	35	40	45
gtc	agc	atc	ggc	tac	ctc	ctg	gtg	aag
50	55	60	65	70	75	80	85	90
gag	ccc	atg	tgc	ccg	gtg	ggc	atg	aac
95	100	105	110	115	120	125	130	135
agc	ctg	ctg	tac	ttc	gag	ggc	cag	gag
140	145	150	155	160	165	170	175	180
ctg	ggg	ctg	gcg	ggc	tcc	tgc	ctg	gca
185	190	195	200	205	210	215	220	225
ttc	ctg	tac	tgc	aac	cct	ggt	gat	gtc
230	235	240	245	250	255	260	265	270
aat	gac	aag	tcc	tac	tgg	ctc	tct	acc
275	280	285	290	295	300	305	310	315
atg	ccc	gtg	gcc	gag	gac	gag	atc	aag
320	325	330	335	340	345	350	355	360
tct	gtg	tgt	gag	gcc	ccg	gcc	atc	gca
365	370	375	380	385	390	395	400	405
gat	gtc	tcc	atc	cca	cac	tgc	cca	gct
410	415	420	425	430	435	440	445	450
atc	gga	tat	tcc	ttc	ctc	atg	cac	acg
455	460	465	470	475	480	485	490	495
ggt	ggc	caa	tca	ctg	gtg	tca	ccg	ggc
500	505	510	515	520	525	530	535	540
cgc	gcc	aca	cca	ttc	atc	gaa	tgc	aat
545	550	555	560	565	570	575	580	585
cac	tac	tac	gcc	aac	aag	tac	agc	ttc
590	595	600	605	610	615	620	625	630
gag	cag	agc	ttc	cag	ggc	tgc	ccc	tcc
635	640	645	650	655	660	665	670	675
ggc	ctc	atc	cgc	aca	cac	atc	agc	cgc
680	<u>aat</u>	<u>ctg</u>	<u>tga</u>					

(SEQ ID NO:5)

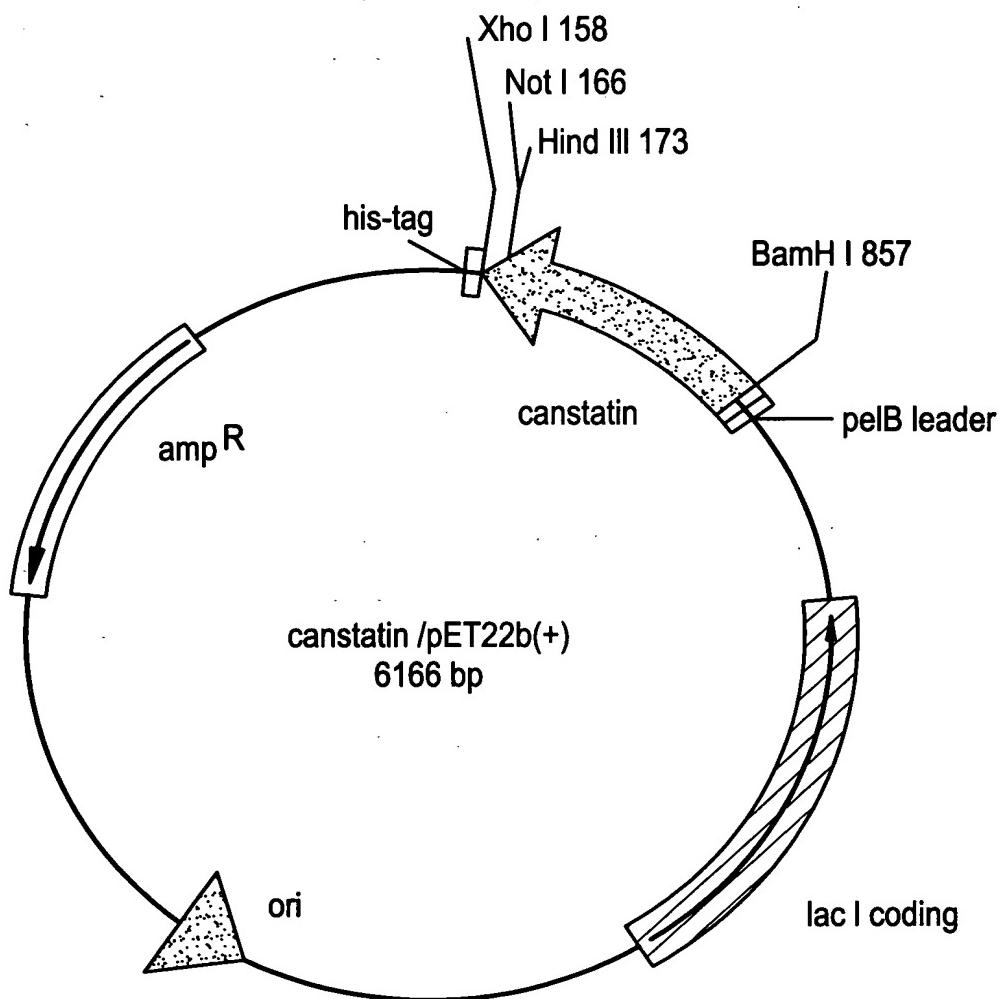
## FIG. 11B

5	10	15	20	25	30	35	40	45						
VSI	GYL	LVK	HSQ	TDQ	EPM	CPV	GMN	KLW	SGY	SLL	YFE	GQE	KAH	NQD
50	55	60	65	70	75	80	85	90						
LGL	AGS	CLA	RFS	TMP	FLY	CNP	GDV	CYY	ASR	NDK	SYW	LST	TAP	LPM
95	100	105	110	115	120	125	130	135						
MPV	AED	EIK	PYI	SRC	SVC	EAP	AIA	IAV	HSQ	DVS	IPH	CPA	GWR	SLW
140	145	150	155	160	165	170	175	180						
IGY	SFL	MHT	AAG	DEG	GGQ	SLV	SPG	SCL	EDF	RAT	PFI	ECN	GGR	GTC
185	190	195	200	205	210	215	220	225						
HYY	ANK	YSF	WLT	TIP	EQS	FQG	SPS	ADT	LKA	GLI	RTH	ISR	CQV	CMK

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NL (SEQ ID NO:6)

FIG. 12



Forward primer: 5'-cgggatccgtcagcatcggtacacc-3'

Reverse primer: 5'-cccaaggcttcaggttttcatgcacac-3'

FIG. 13A

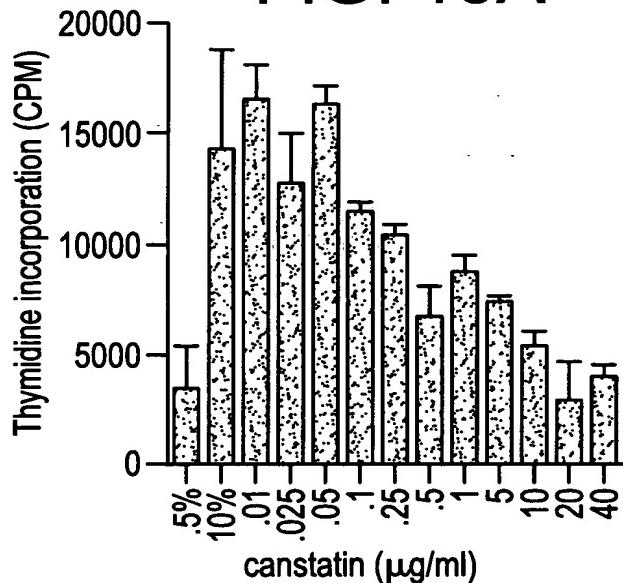


FIG. 13B

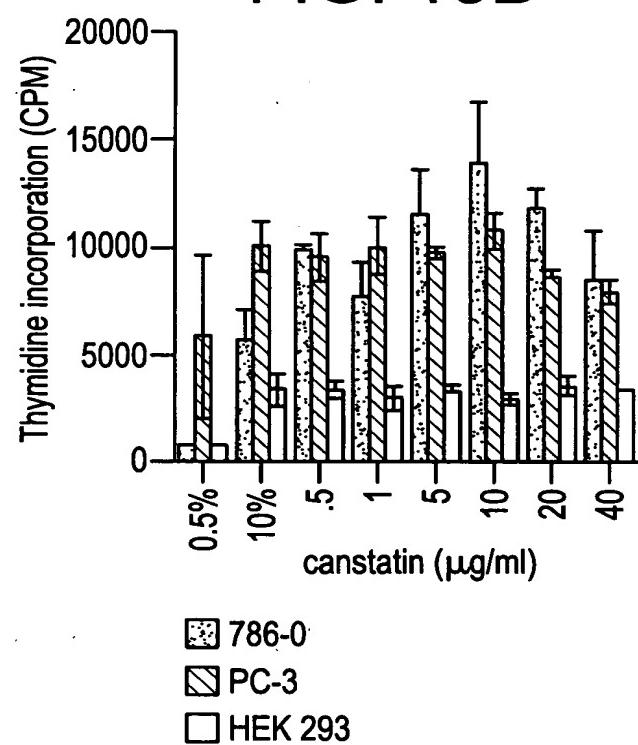


FIG. 13C

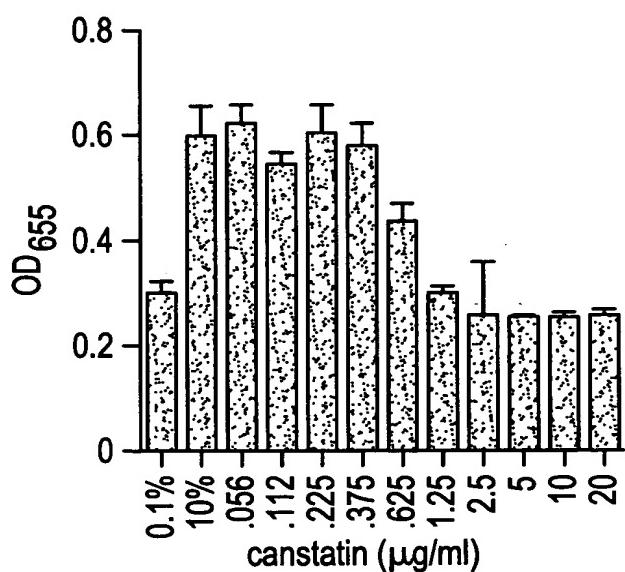


FIG. 13D

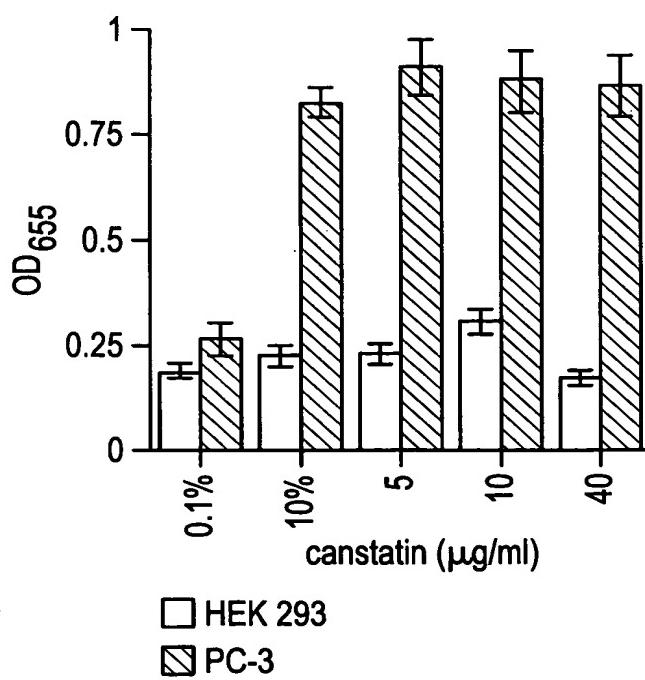


FIG. 14

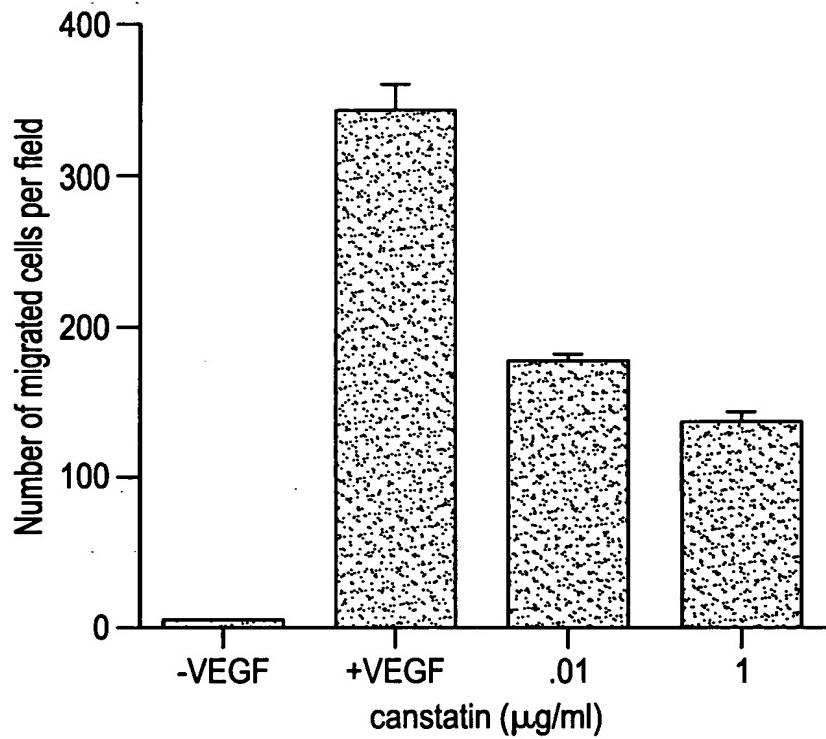
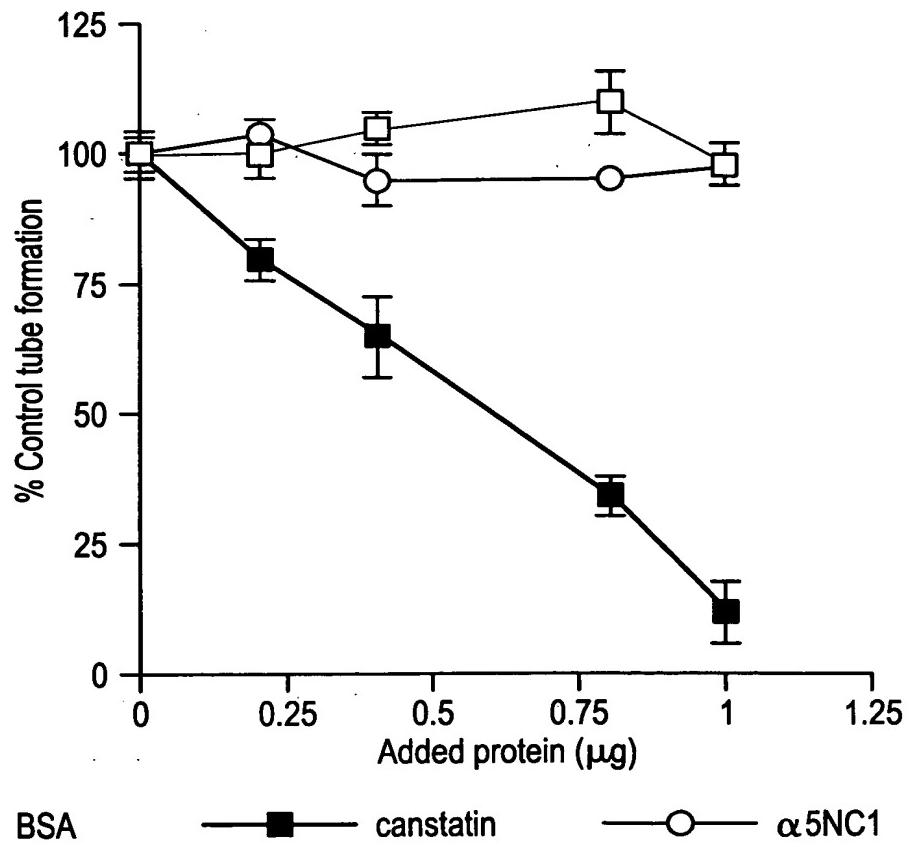
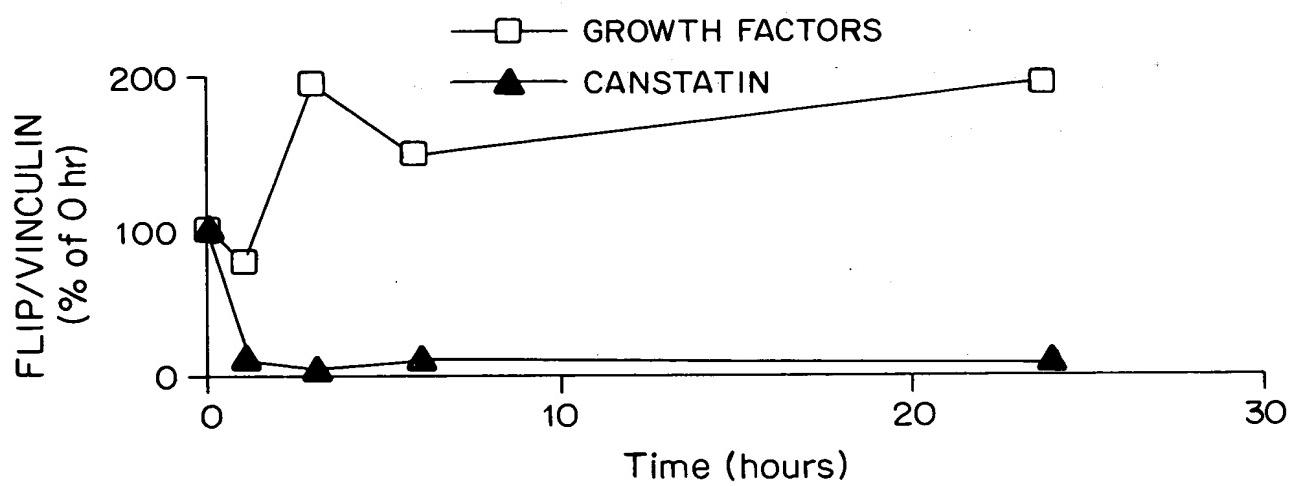
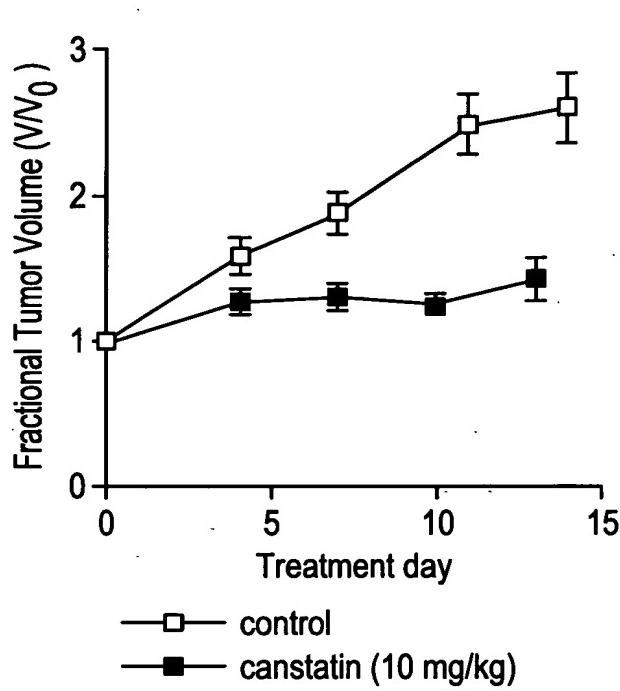
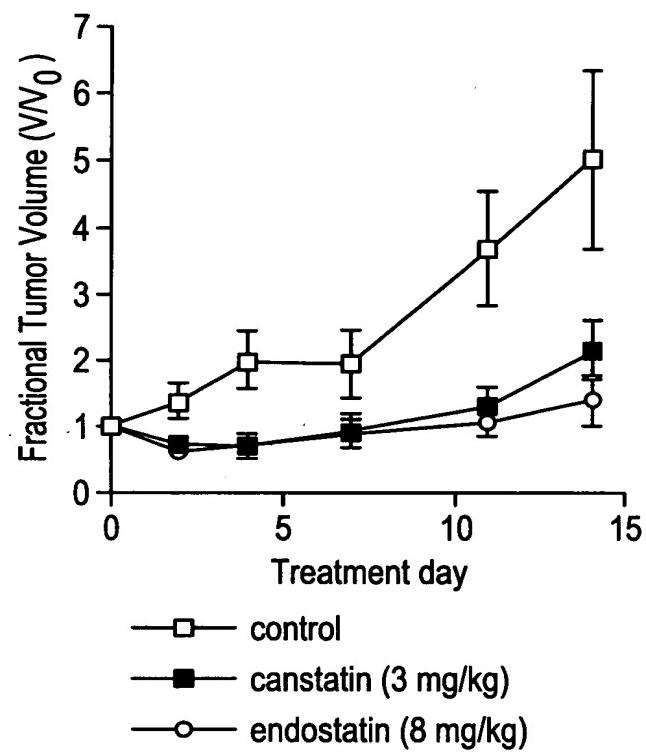
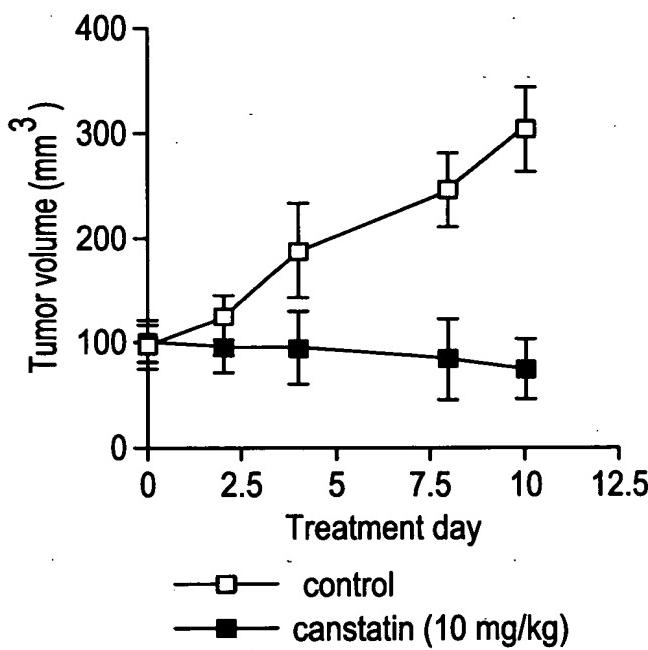
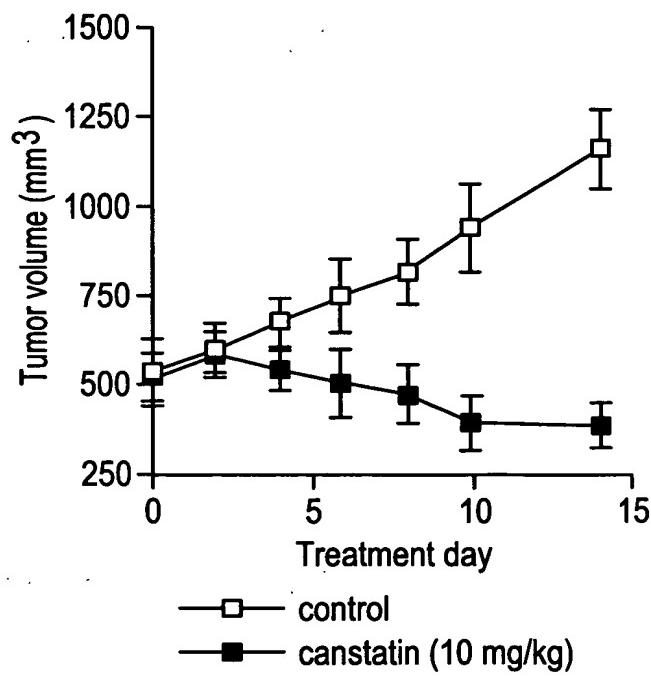


FIG. 15



**FIG. 16**

**FIG. 17A****FIG. 17B****FIG. 17C****FIG. 17D**

## FIG. 18A

pET22b(+) forward primer:

5'-CGGGAT CCA GGT TTG AAA GGA AAA CGT-3' (SEQ ID NO:11)

pET22b(+) reverse primer:

5'-CCCAAGCTT TCA GTG TCT TTT CTT CAT-3' (SEQ ID NO:12)

5	10	15	20	25	30	35	40	45						
cca	qgt	ttq	aaa	qqa	aaa	cqt	gga	gac	agt	gga	tca	cct	gca	acc
50	55	60	65	70	75	80	85	90						
tgg	aca	acg	aga	ggc	ttt	gtc	ttc	acc	cga	cac	agt	caa	acc	aca
95	100	105	110	115	120	125	130	135						
gca	att	cct	tca	tgt	cca	gag	ggg	aca	gtg	cca	ctc	tac	agt	ggg
140	145	150	155	160	165	170	175	180						
ttt	tct	ttt	ctt	ttt	gta	caa	gga	aat	caa	cga	gcc	cac	gga	caa
185	190	195	200	205	210	215	220	225						
gac	ctt	gga	act	ctt	ggc	agc	tgc	ctg	cag	cga	ttt	acc	aca	atg
230	235	240	245	250	255	260	265	270						
cca	ttc	tta	ttc	tgc	aat	gtc	aat	gat	gta	tgt	aat	ttt	gca	tct
275	280	285	290	295	300	305	310	315						
cga	aat	gat	tat	tca	tac	tgg	ctg	tca	aca	cca	gct	ctg	atg	cca
320	325	330	335	340	345	350	355	360						
atg	aac	atg	gct	ccc	att	act	ggc	aga	gcc	ctt	gag	cct	tat	ata
365	370	375	380	385	390	395	400	405						
agc	aga	tgc	act	gtt	tgt	gaa	ggt	cct	gcg	atc	gcc	ata	gcc	gtt
410	415	420	425	430	435	440	445	450						
cac	agc	caa	acc	act	gac	att	cct	cca	tgt	cct	cac	ggc	tgg	att
455	460	465	470	475	480	485	490	495						
tct	ctc	tgg	aaa	gga	ttt	tca	ttc	atc	atg	ttc	aca	agt	gca	ggt
500	505	510	515	520	525	530	535	540						
tct	gag	ggc	acc	ggg	caa	gca	ctg	gcc	tcc	cct	ggc	tcc	tgc	ctg
545	550	555	560	565	570	575	580	585						
gaa	gaa	ttc	cga	gcc	agc	cca	ttt	cta	gaa	tgt	cat	gga	aga	gga
590	595	600	605	610	615	620	625	630						
acg	tgc	aac	tac	tat	tca	aat	tcc	tac	agt	ttc	tgg	ctg	gct	tca
635	640	645	650	655	660	665	670	675						
tta	aac	cca	gaa	aga	atg	ttc	aga	aag	cct	att	cca	tca	act	gtg
680	685	690	695	700	705	710	715	720						
aaa	gct	ggg	gaa	tta	gaa	aaa	ata	ata	agt	cgc	tgt	cag	gtg	tgc
725	730	735												
<u>atq aaq aaa aga cac tqa</u> (SEQ ID NO:9)														

pET22b- $\alpha$ 3(IV) NC1 = nucleotides 4 through 735

Tumstatin 333 = nucleotides 4 through 375

Tumstatin 334 - nucleotide 376 through 735

## FIG. 18B

\*  
5 10 15 20 25 30 35 40 45  
PGL KGK RGD SGS PAT WTT RGF VFT RHS QTT AIP SCP EGT VPL YSG  
  
50 55 60 65 70 75 80 85 90  
FSF LFV QGN QRA HGQ DLG TLG SCL QRF TTM PFL FCN VND VCN FAS  
  
95 100 105 110 115 120 125 130 135  
RND YSY WLS TPA LMP MNM API TGR ALE PYI SRC TVC EGP AIA IAV  
  
140 145 150 155 160 165 170 175 180  
HSQ TTD IPP CPH GWI SLW KGF SFI MFT SAG SEG TGQ ALA SPG SCL  
  
185 190 195 200 205 210 215 220 225  
EEF RAS PFL ECH GRG TCN YYF NSY SFW LAS LNP ERM FRK PIP STV  
  
230 235 240 245  
KAG ELE KII SRC QVC MKK RH +  
(SEQ ID NO:10)

pET22b  $\alpha$ 3(IV) NC1 = residues 2 through 245

Tumstatin 333 = residues 2 through 125

Tumstatin 334 = residues 126 through 245

FIG. 19

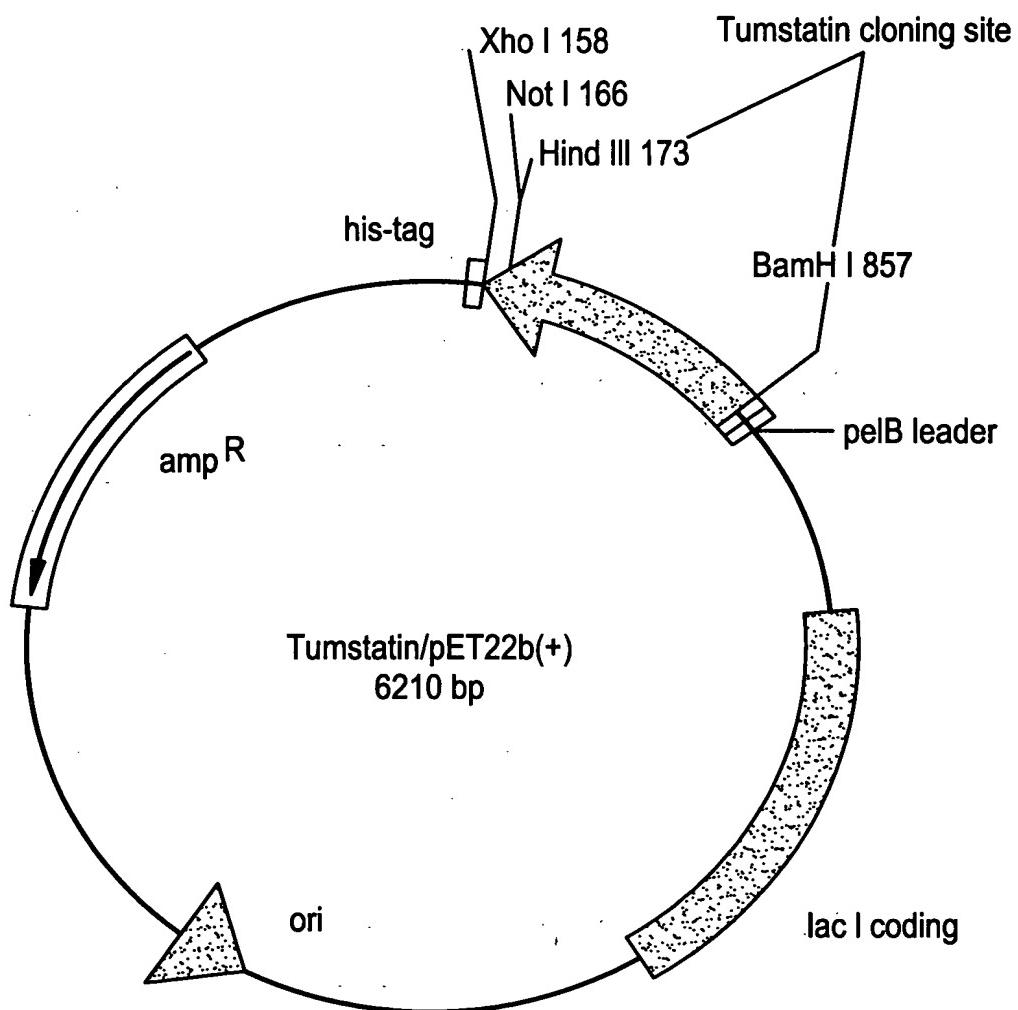


FIG. 20

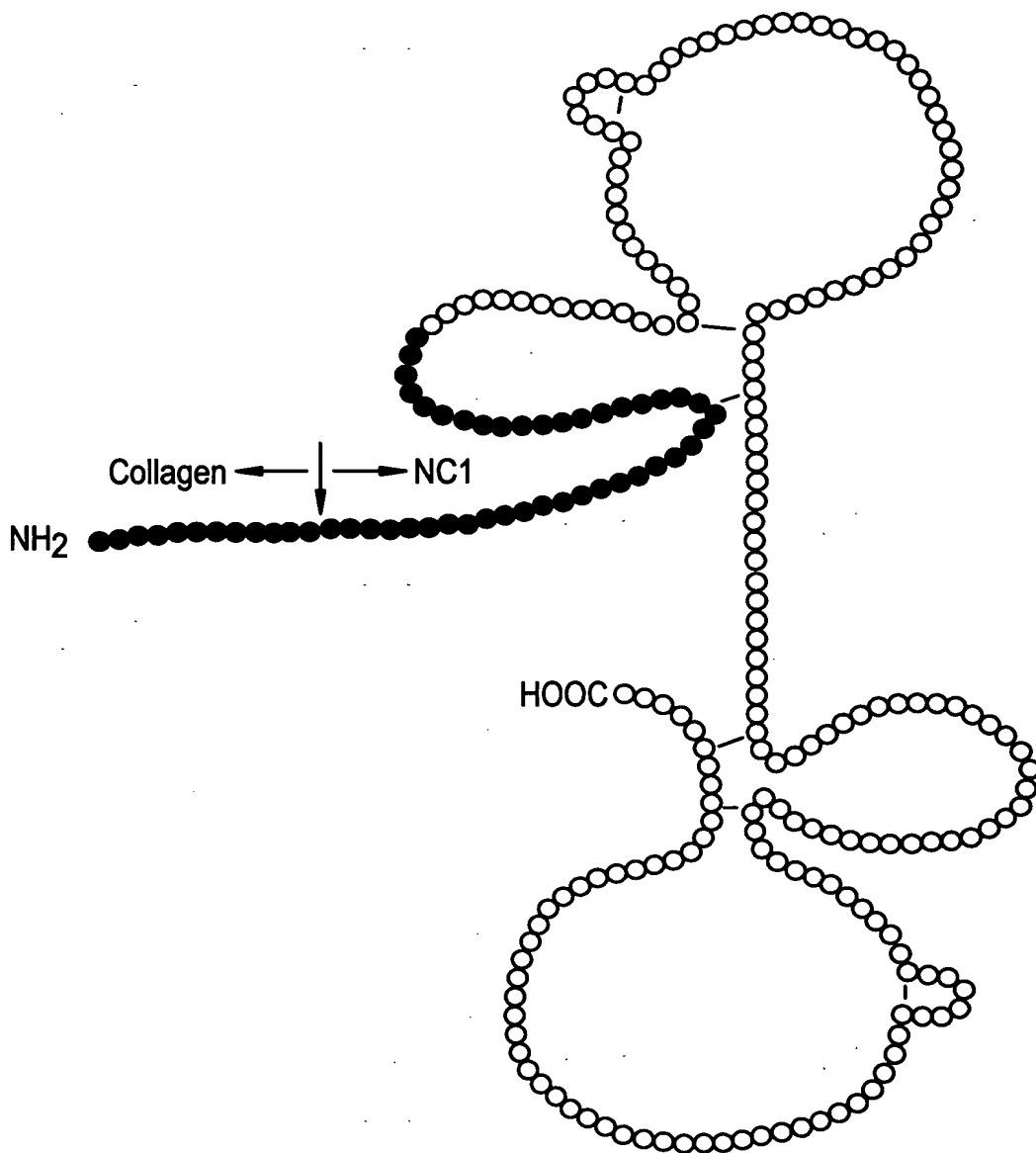
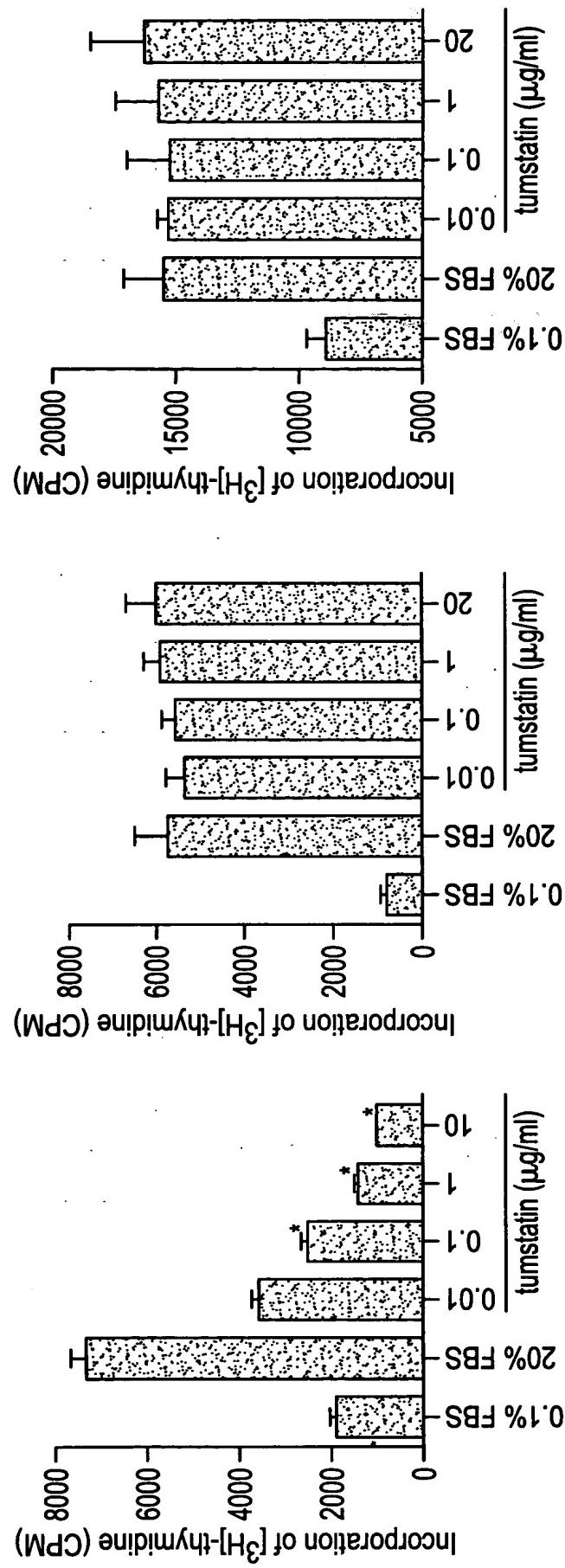


FIG. 21A  
FIG. 21B  
FIG. 21C



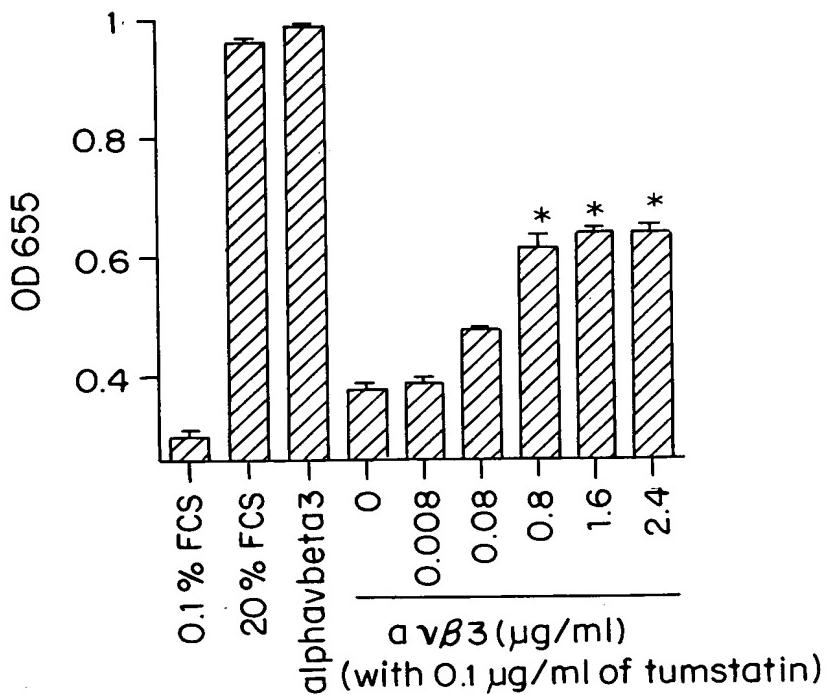


FIG. 22

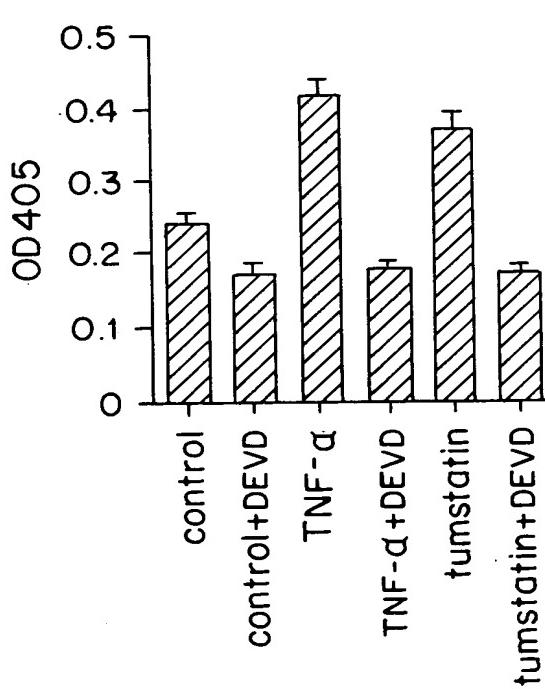


FIG. 23A

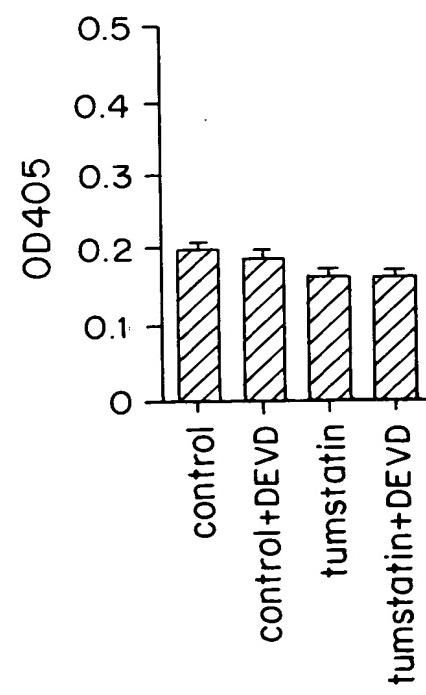


FIG. 23B

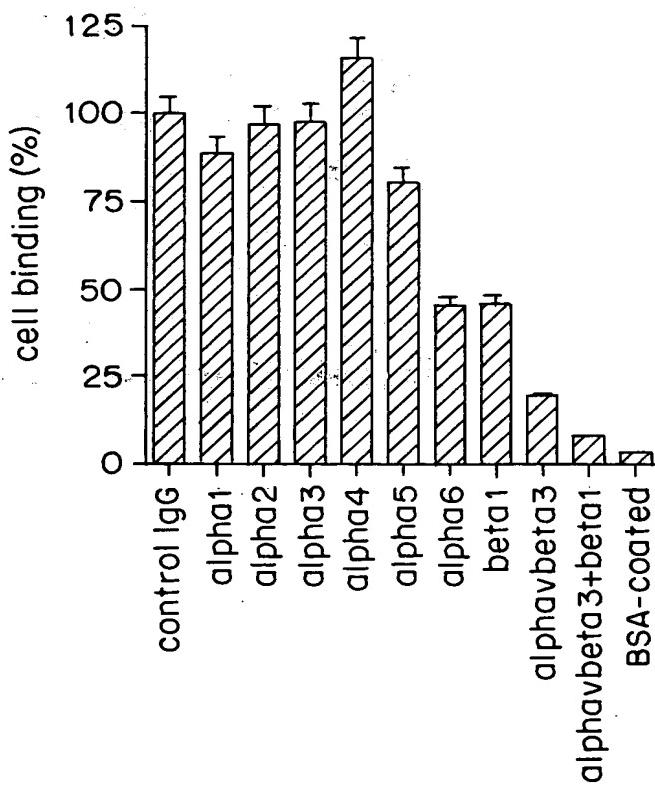


FIG. 24A

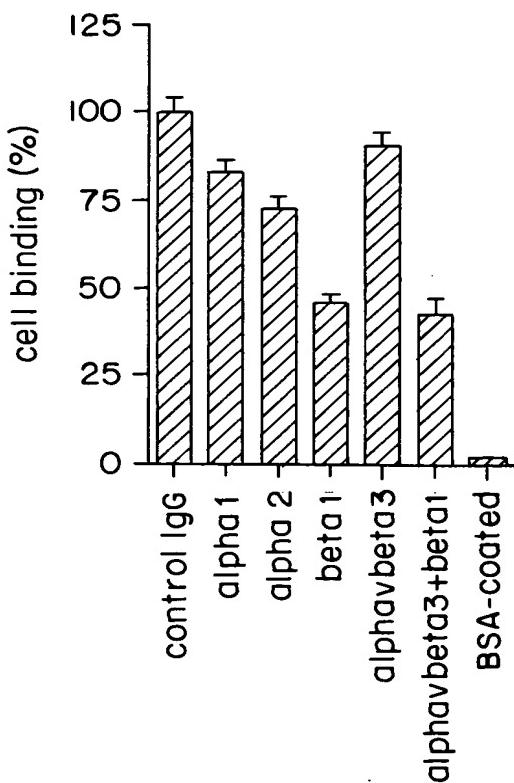


FIG. 24B

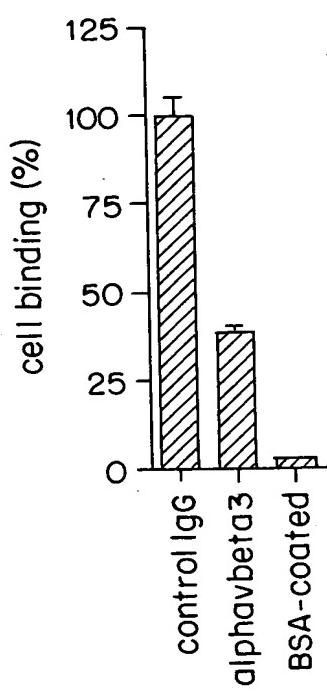


FIG. 24C

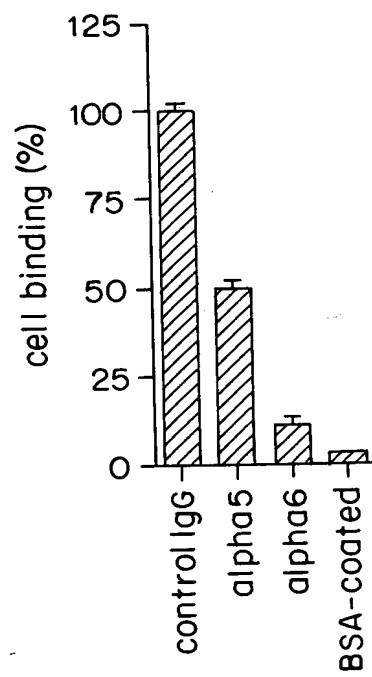


FIG. 24D

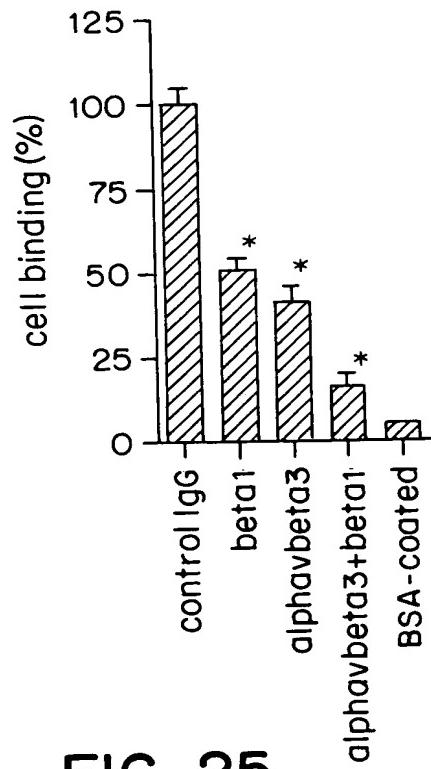


FIG. 25

FIG. 26

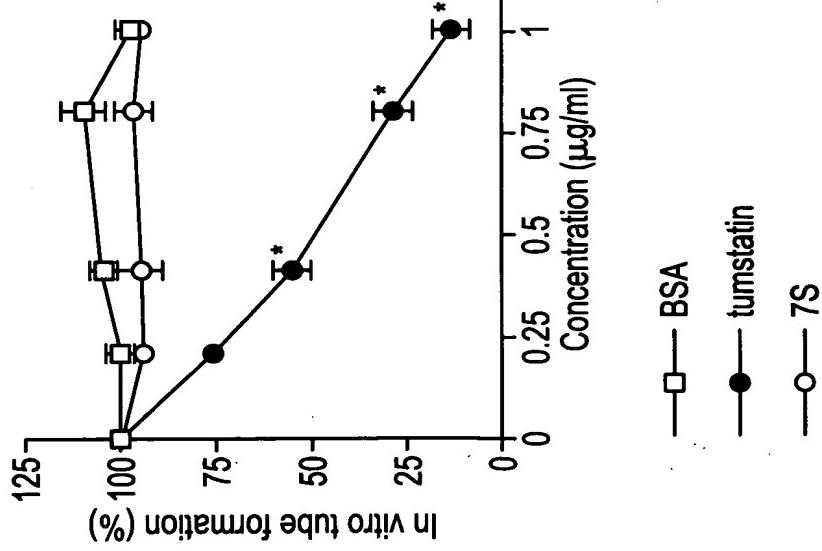


FIG. 27A

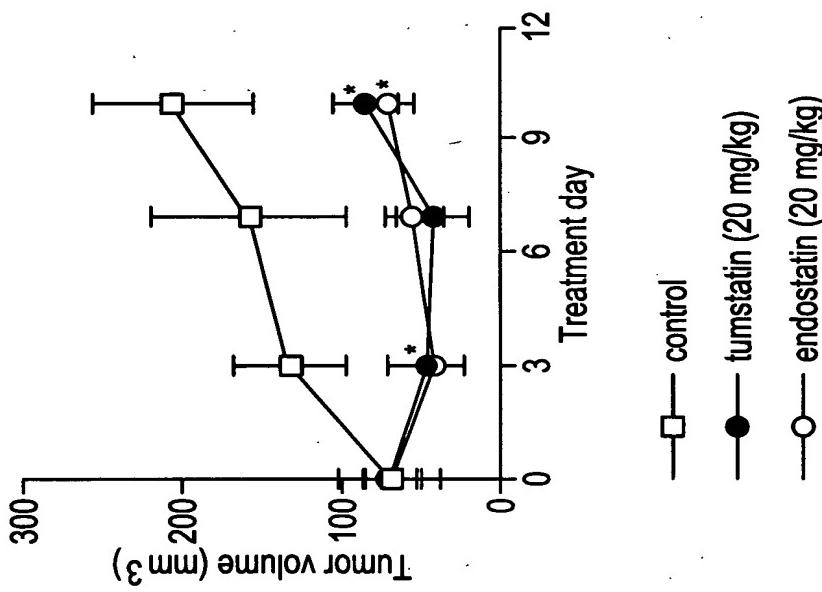


FIG. 27B

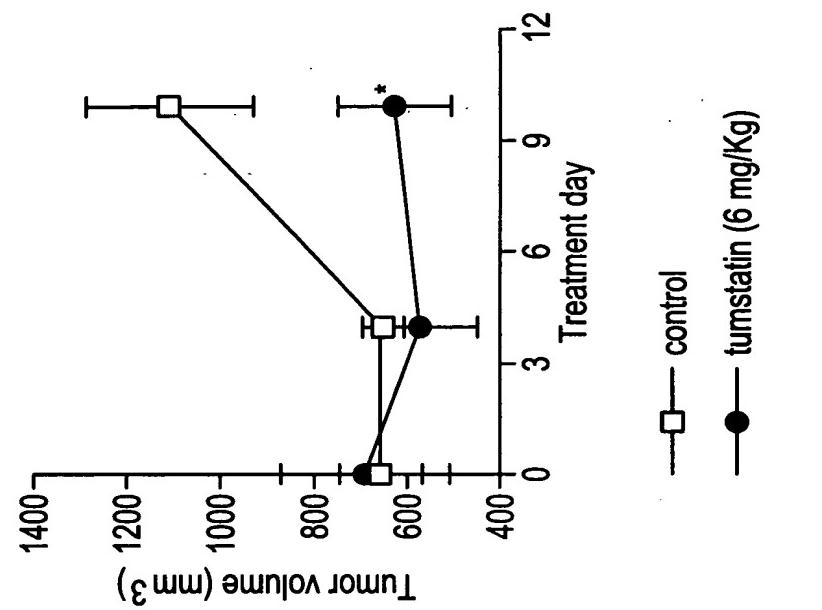
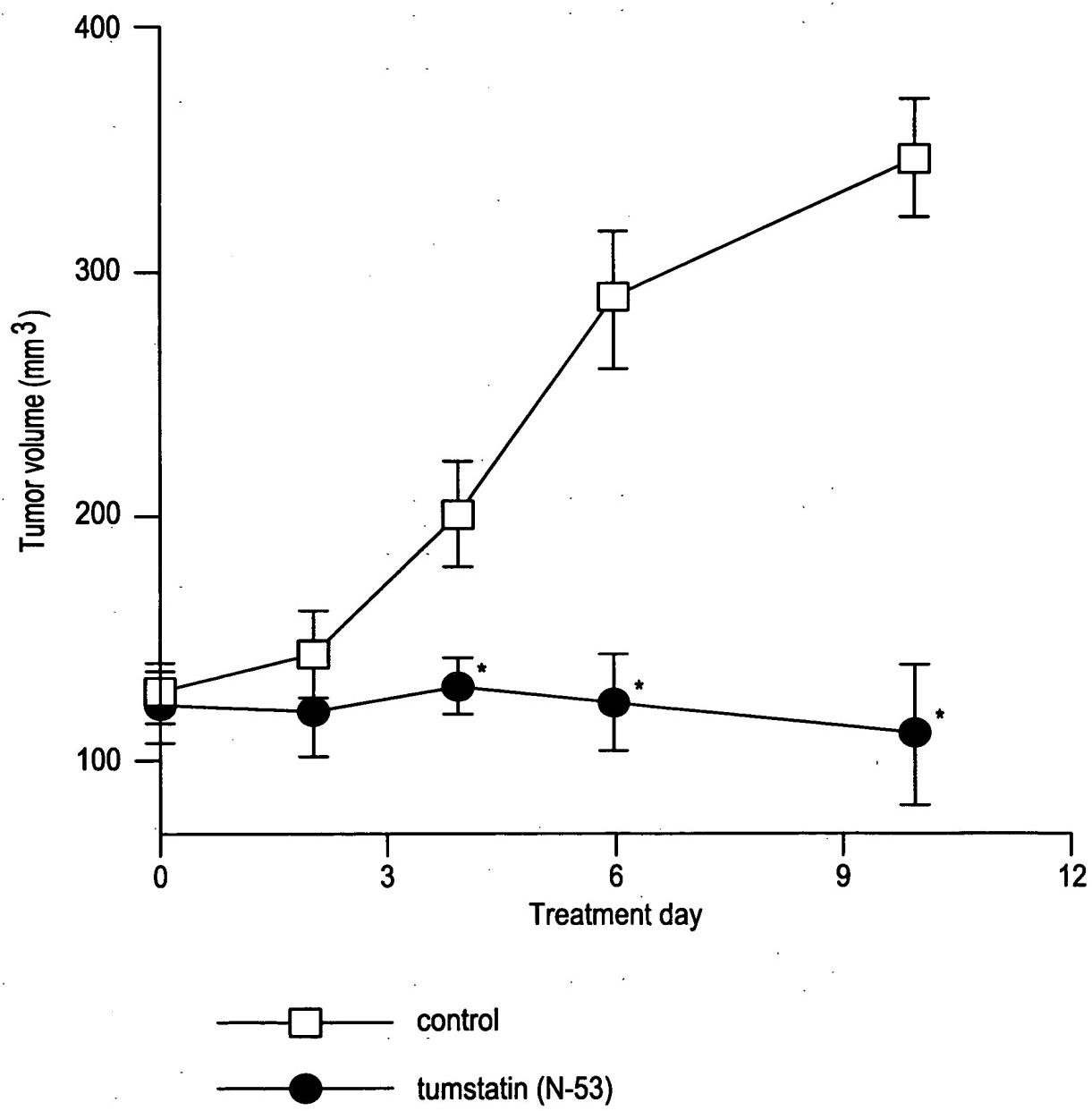


FIG. 28



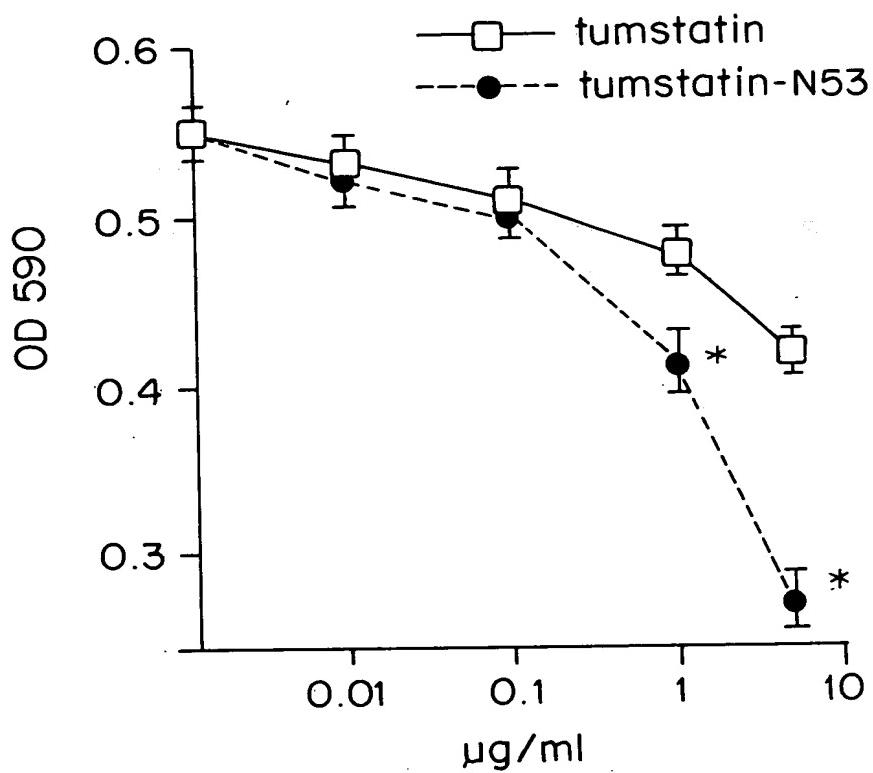


FIG. 29

FIG. 30

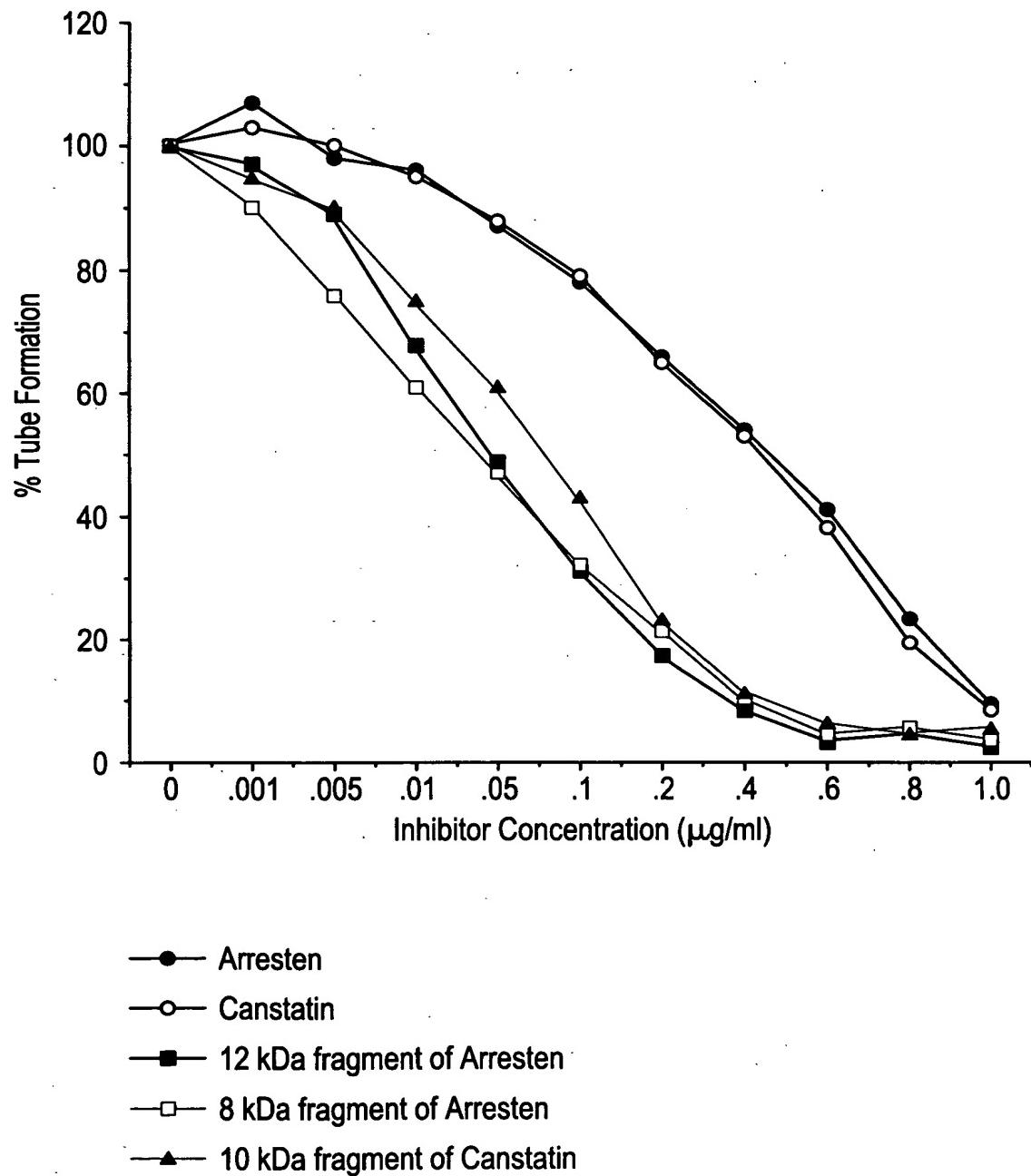
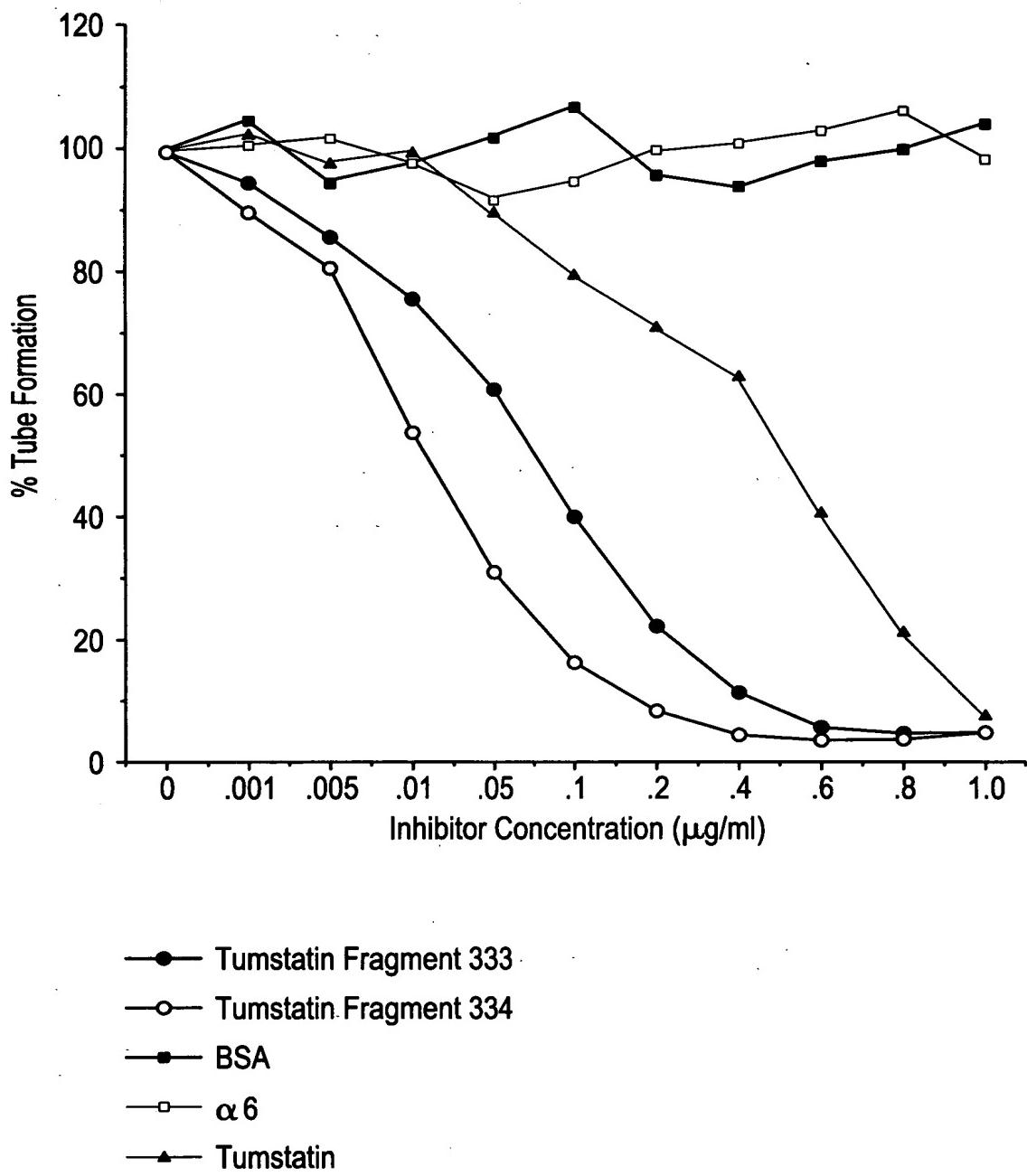
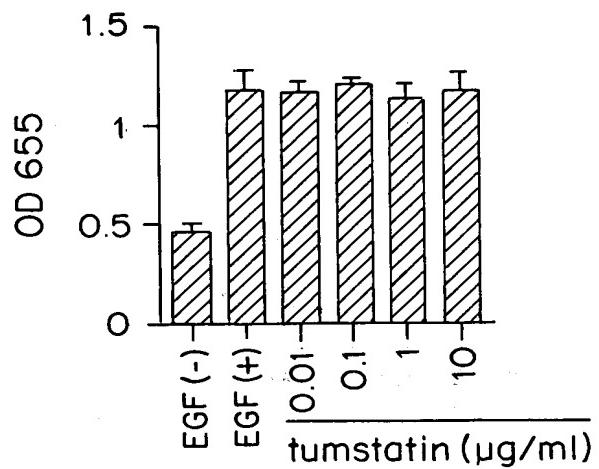
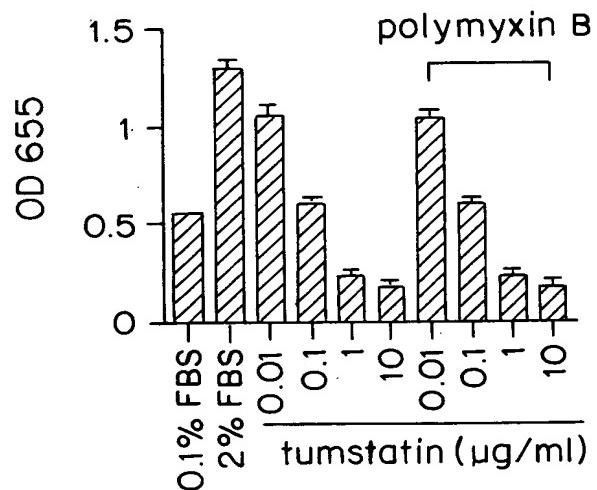


FIG. 31

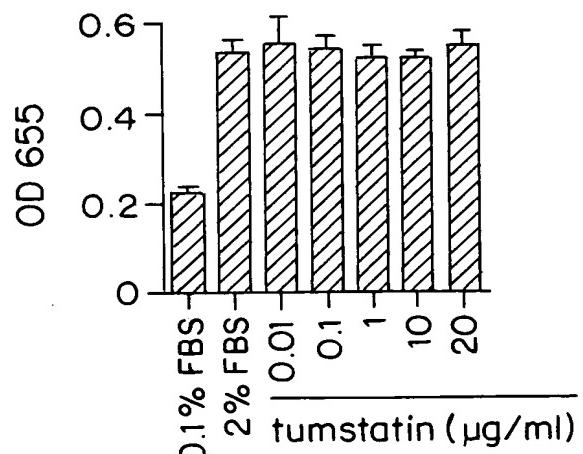




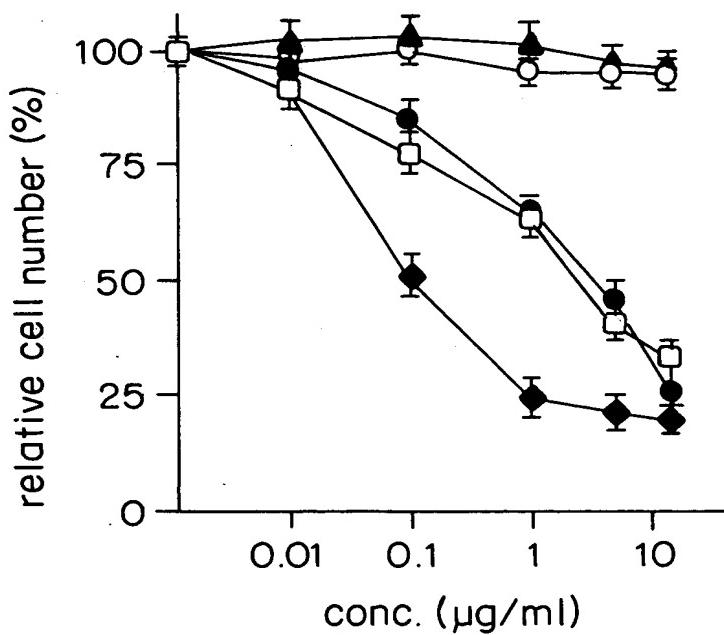
**FIG. 32A**



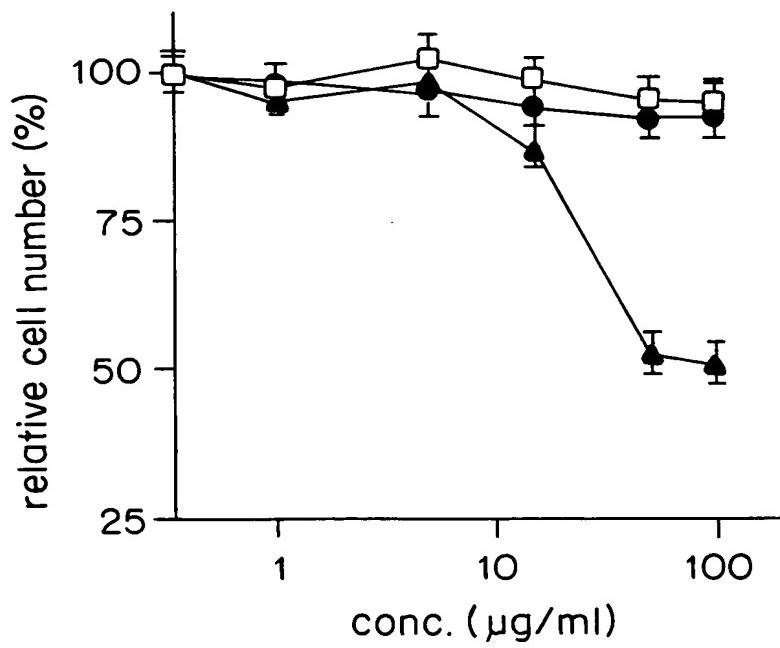
**FIG. 32B**



**FIG. 32C**



**FIG. 33A**



**FIG. 33B**

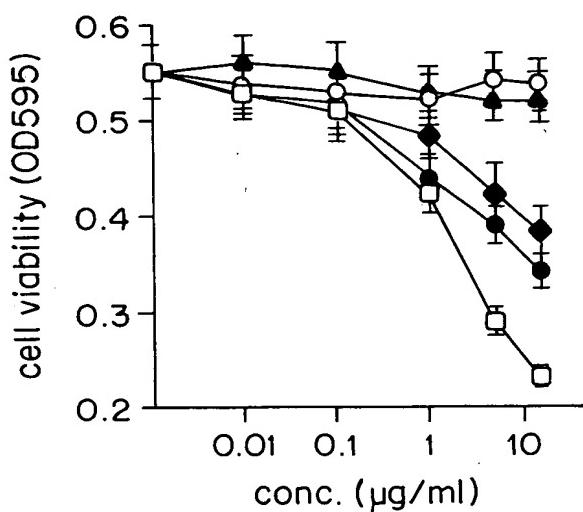


FIG. 34A

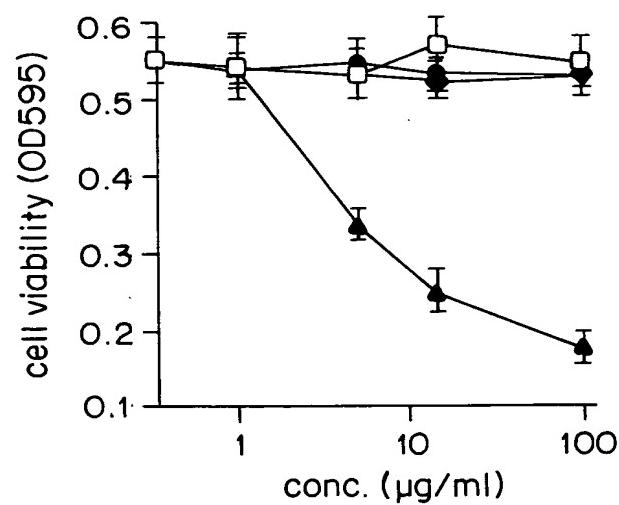


FIG. 34B

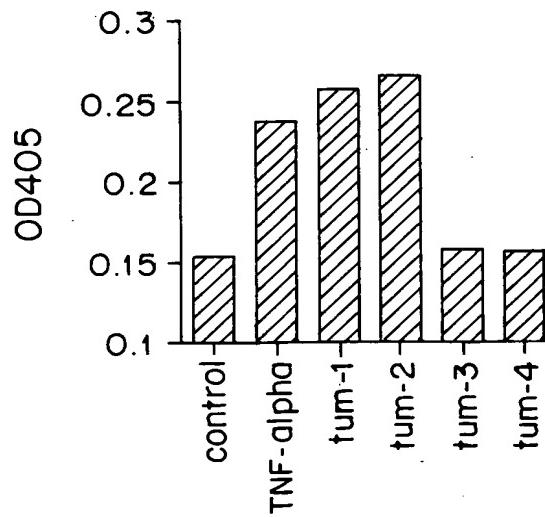


FIG. 35

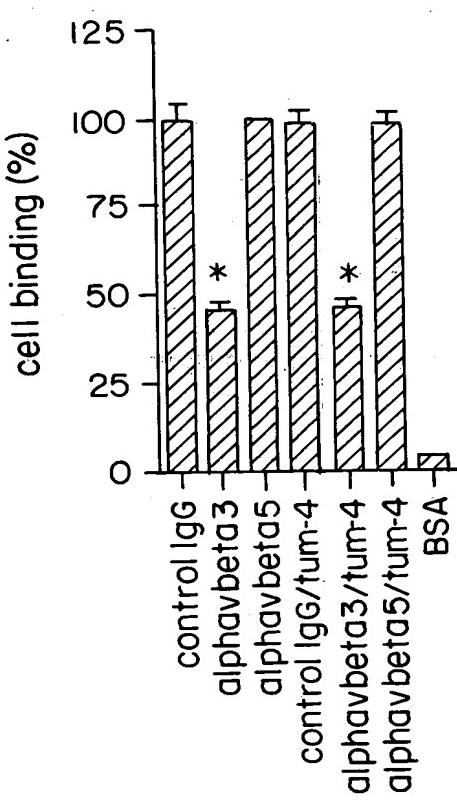


FIG. 36A

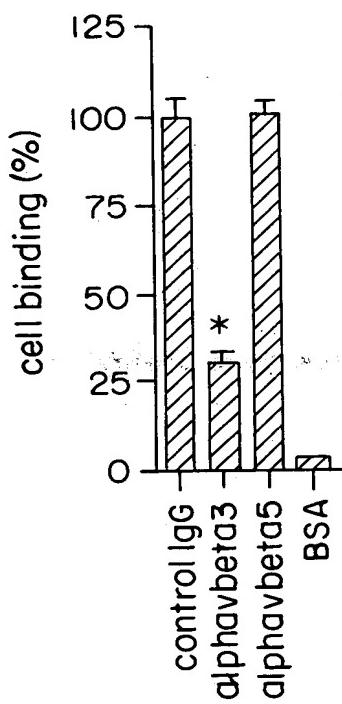


FIG. 36B

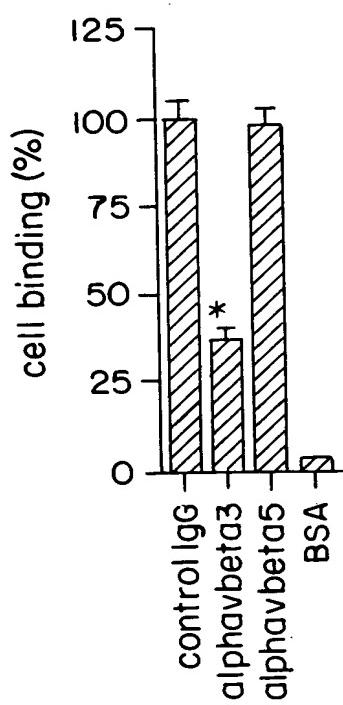


FIG. 36C

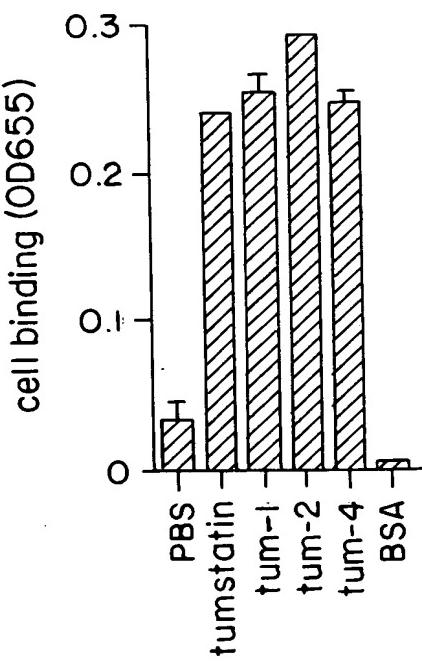


FIG. 37

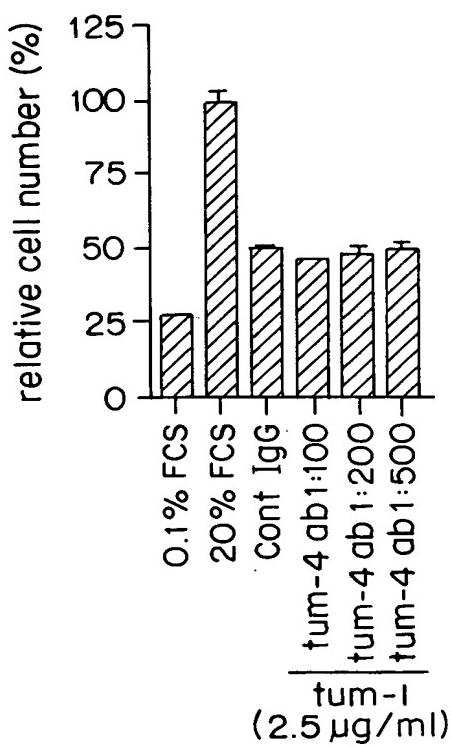


FIG. 38A

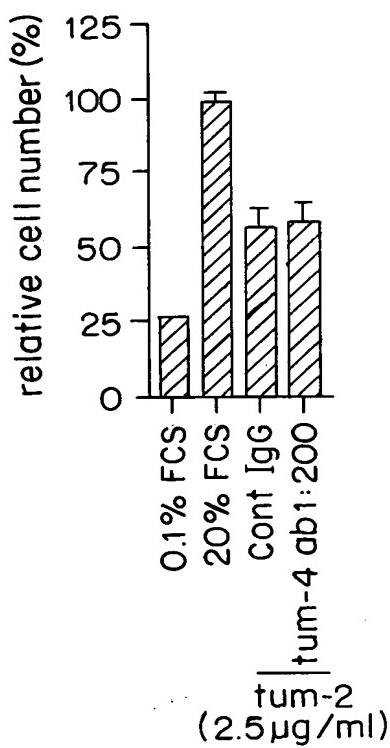


FIG. 38B

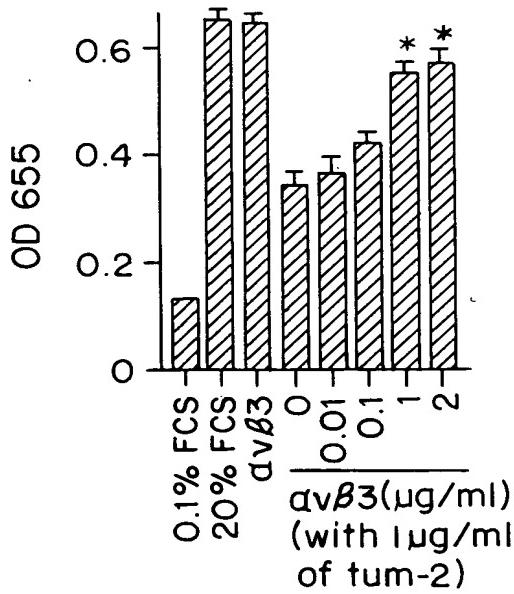


FIG. 38C

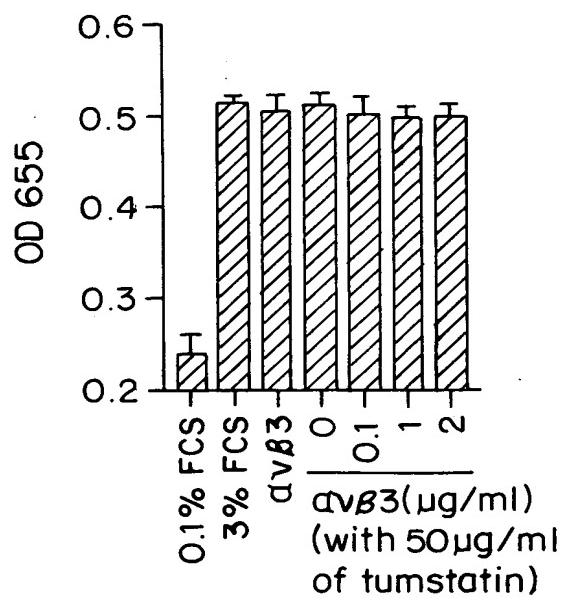


FIG. 38D

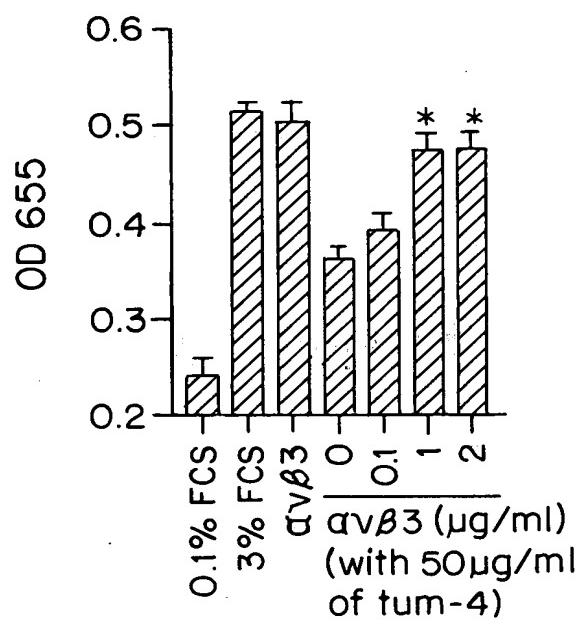


FIG. 38E

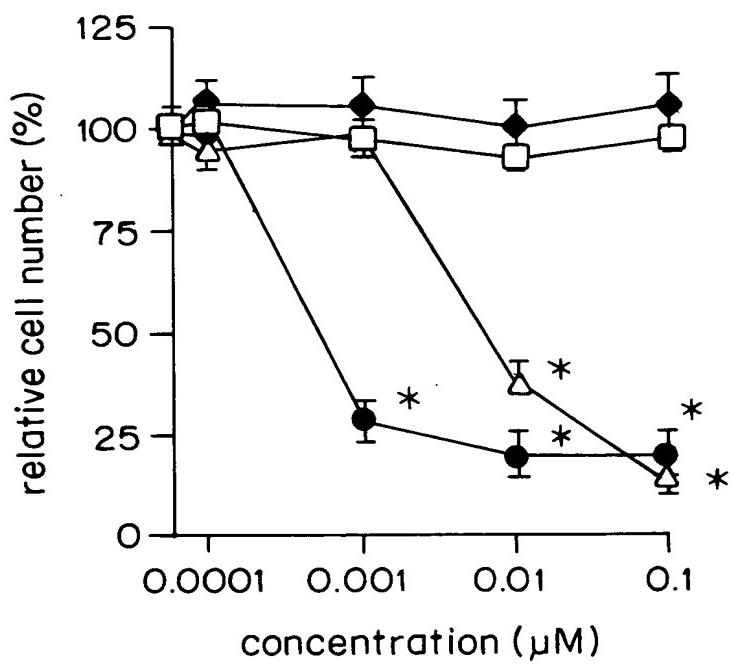


FIG. 39

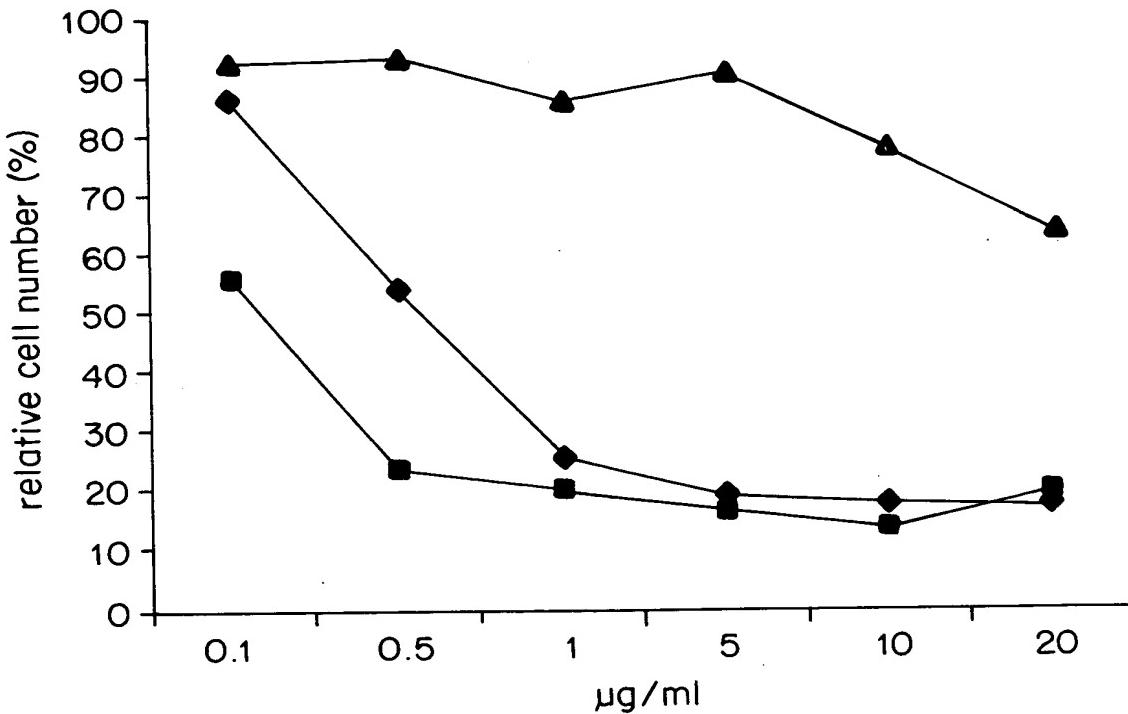


FIG. 40

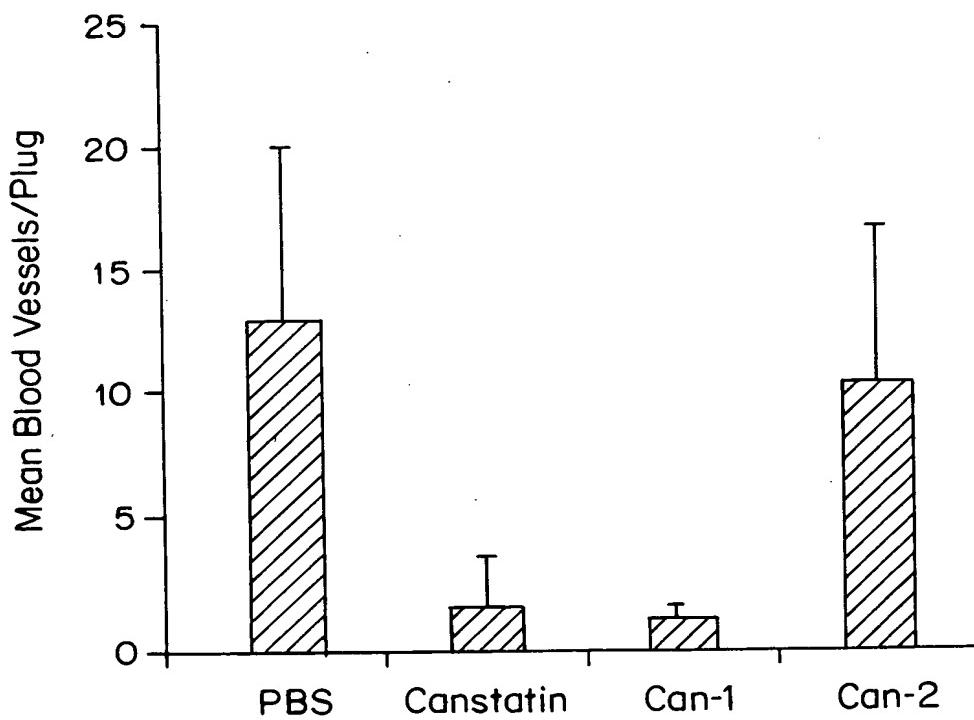


FIG. 41

## FIG. 42

**T1**

**GP-A**

PGLKGK**RGD**SGSPATWTTTRGFVFTRHSQT**TAIPSCPEGTVP**LY

**T3**

**T2**

**T4**

SGFSFLFVQGNQRAHGQDLGTLGSCLQRFTT~~MPFLFCNVNDVC~~

**T3**

**T5**

**T6**

**T4**

NFASRNDYSYWLSTPALMPMNMAPITGRALEPYISRCTVCEGP

**T6**

**GP-B**

AIAIAVHSQT**TDI**PPCPHG**WISL**WKGSFIMFTSAGSEGTGQA  
LASPGSCLEEFRASP~~F~~LECHGRGTCNYSNSYSFWLASLNPER  
MFRKPIPSTVKAGELEKIIISRCQVCMKKRH

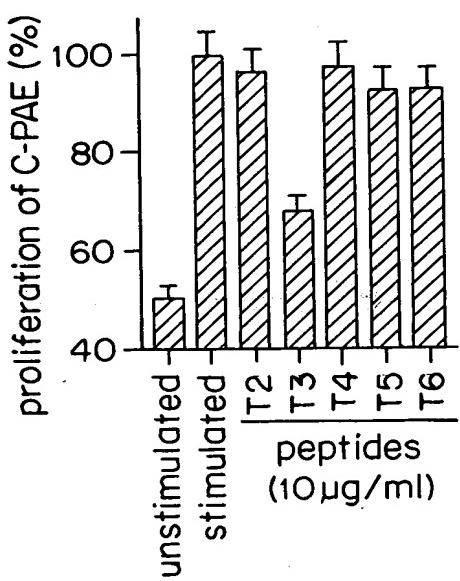


FIG. 43A

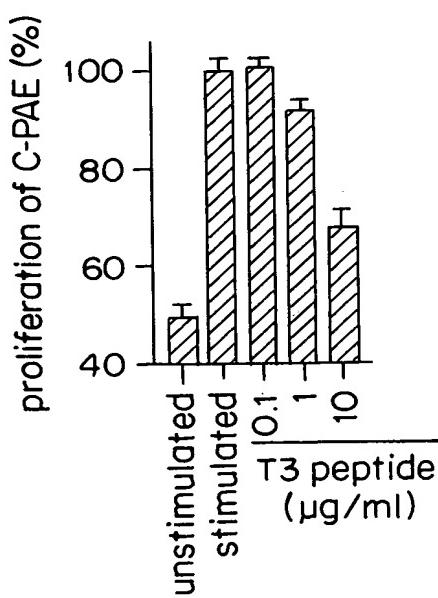


FIG. 43B

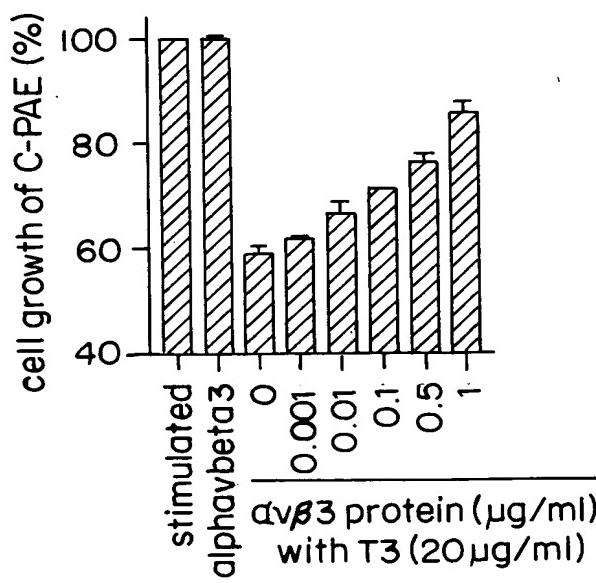


FIG. 43C

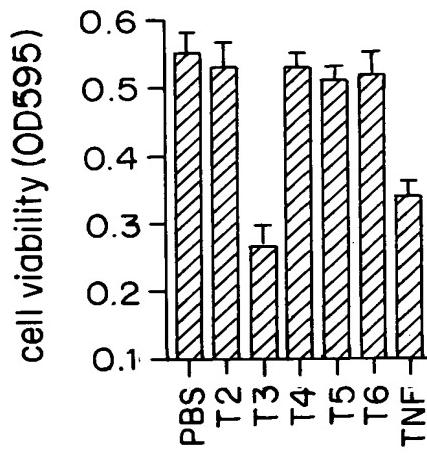


FIG. 43D

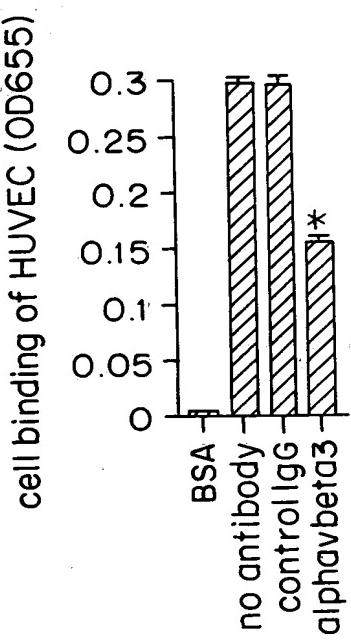


FIG. 44A

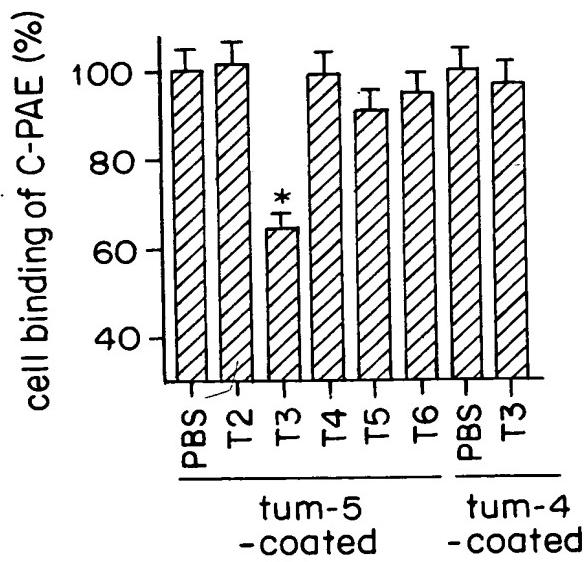


FIG. 44C

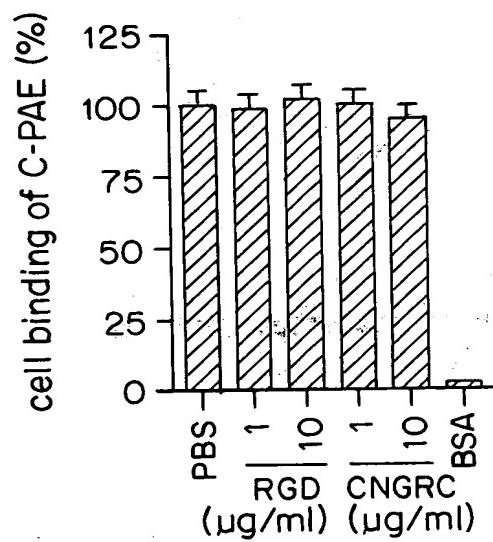


FIG. 44B

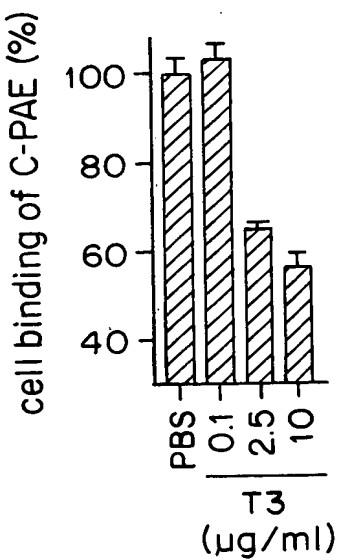


FIG. 44D

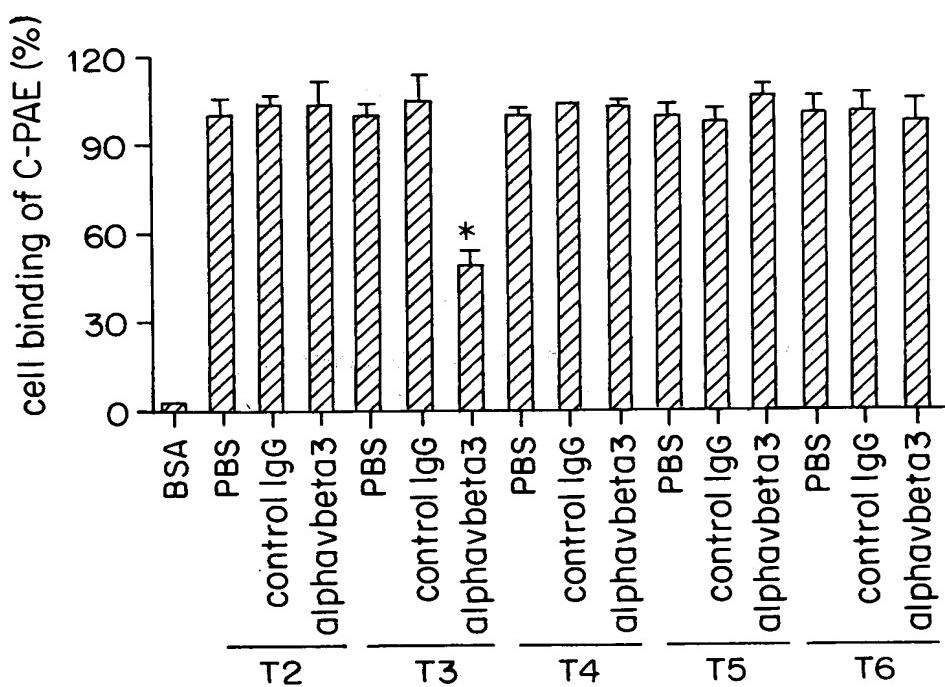


FIG. 44E

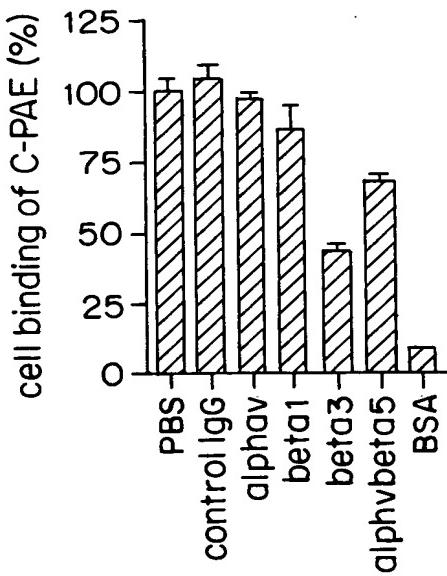


FIG. 44F

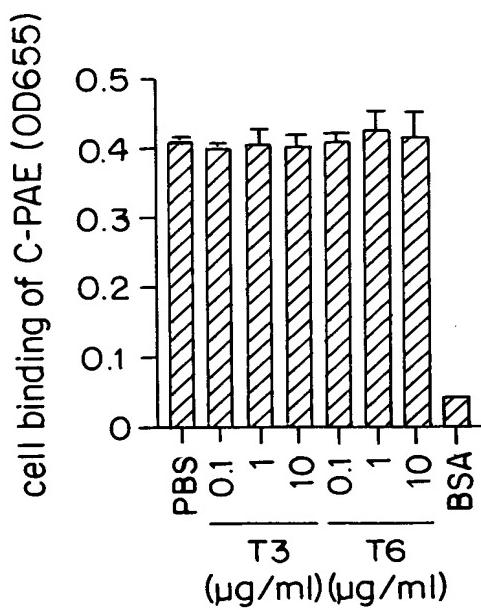
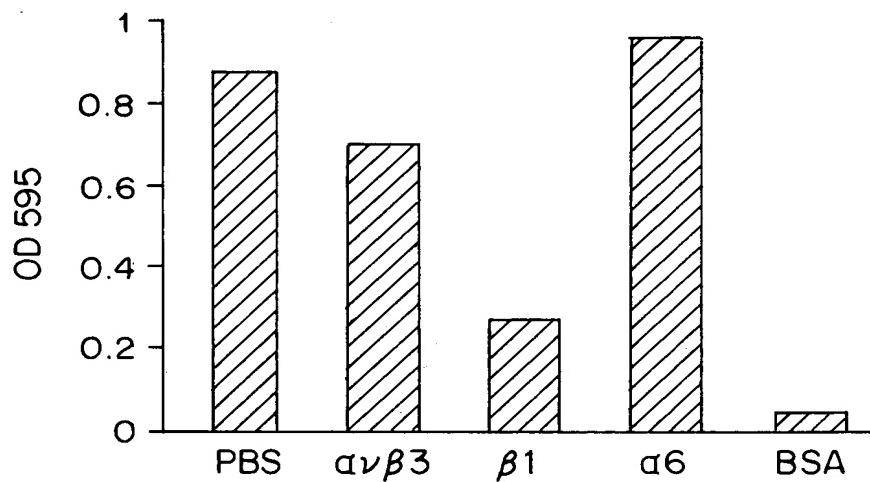
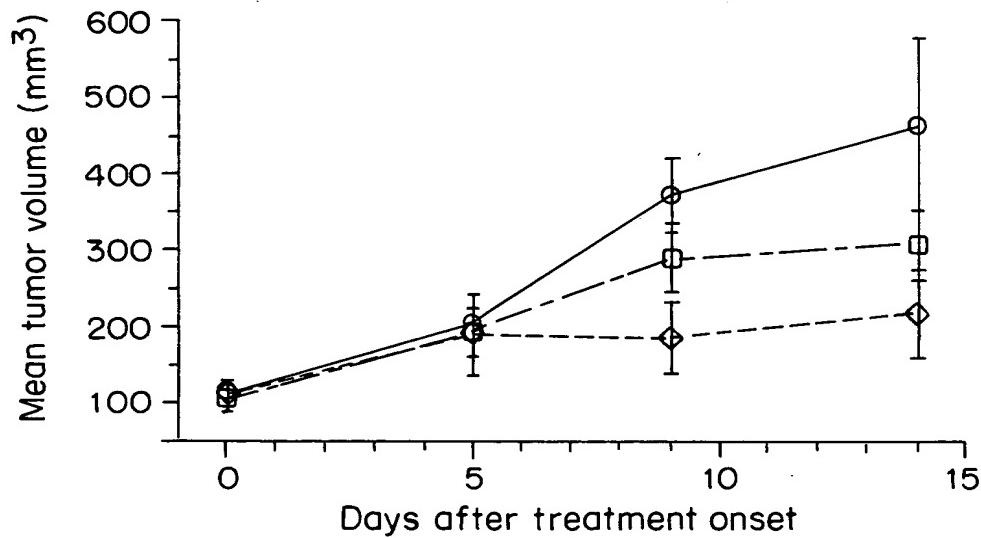


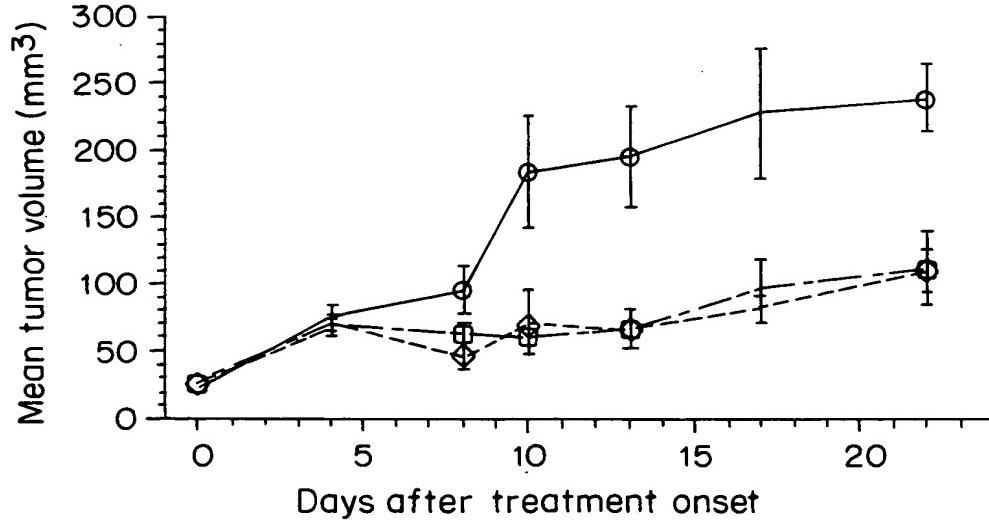
FIG. 44G



**FIG. 45**



**FIG. 46**



**FIG. 47**

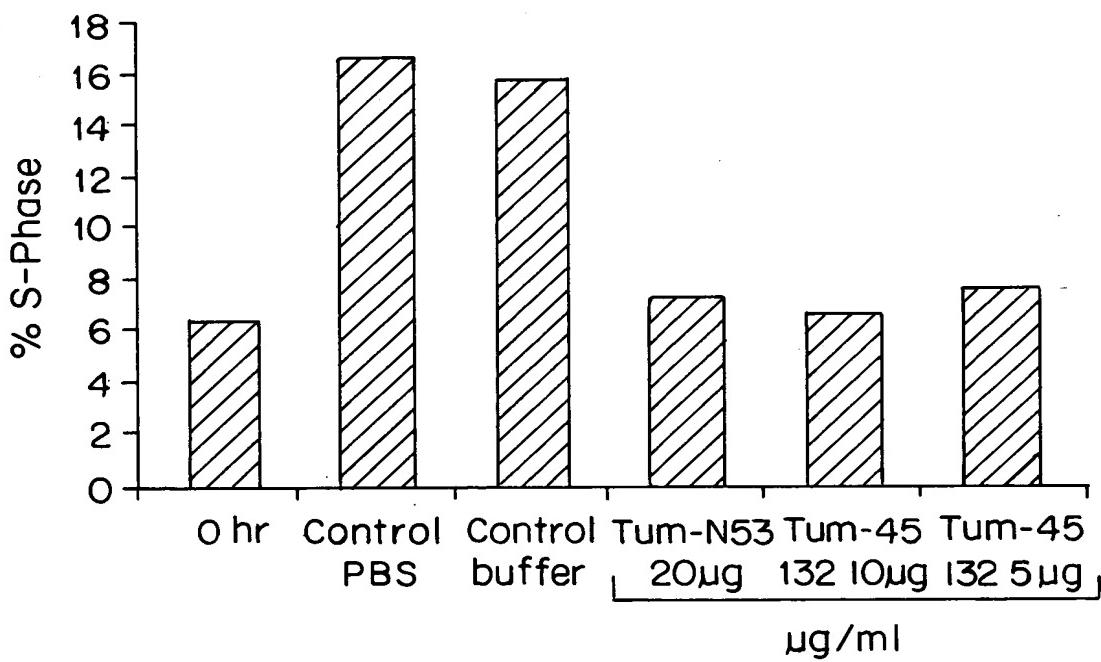


FIG. 48

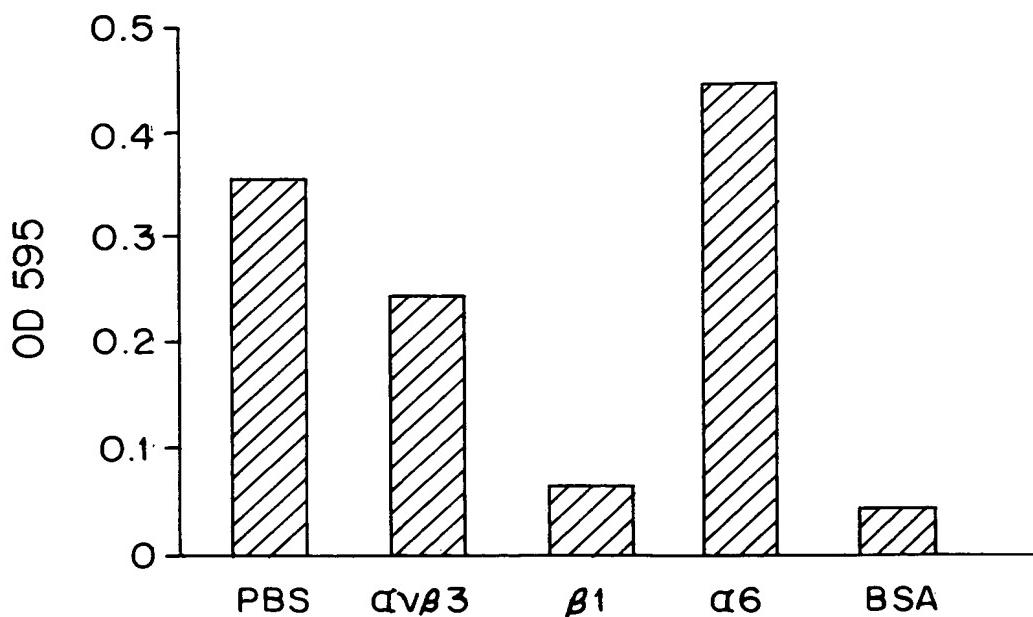


FIG. 49

Fig. 50

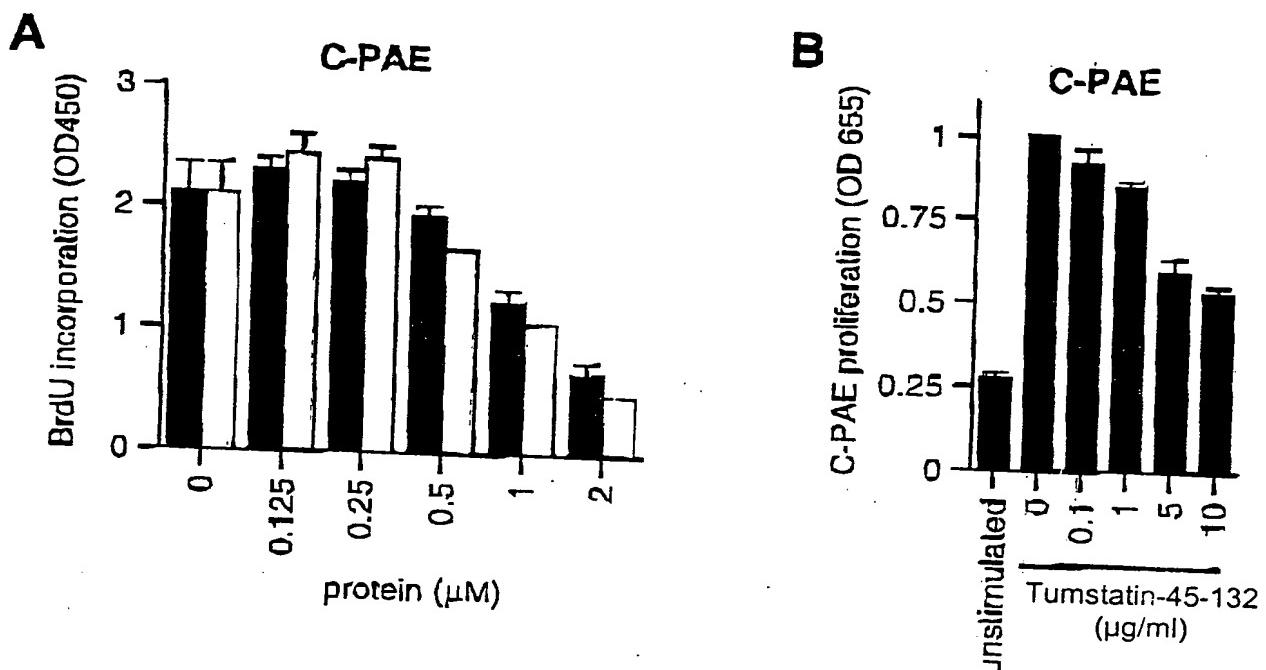


Fig. 51

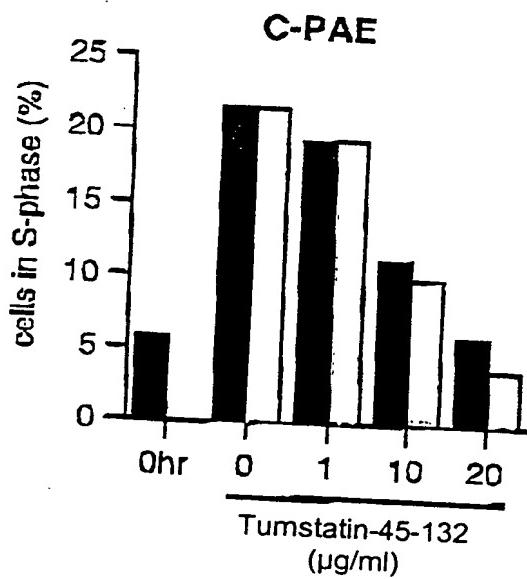
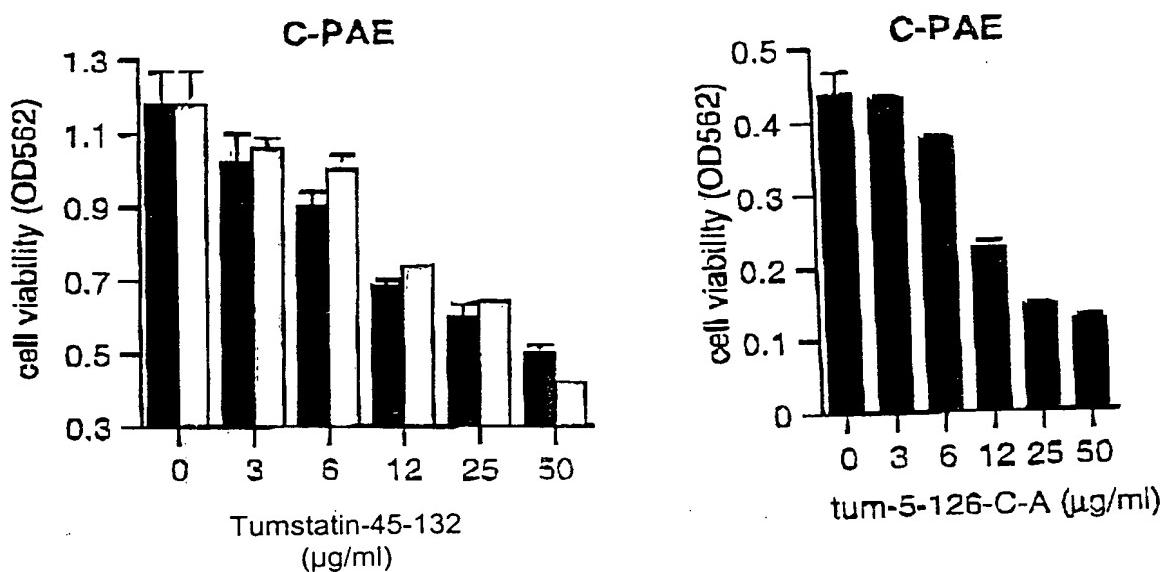


Fig. 52

A

B



C

D

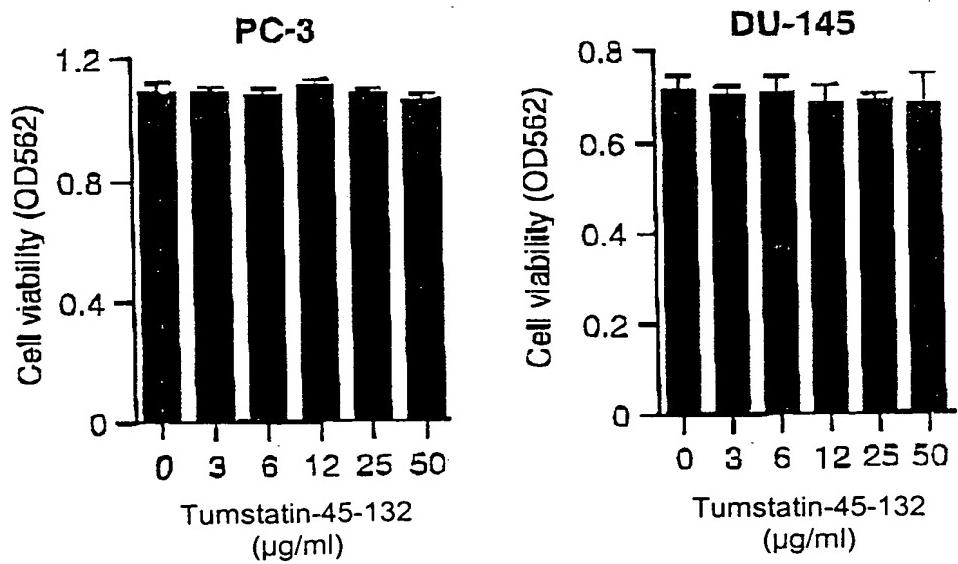
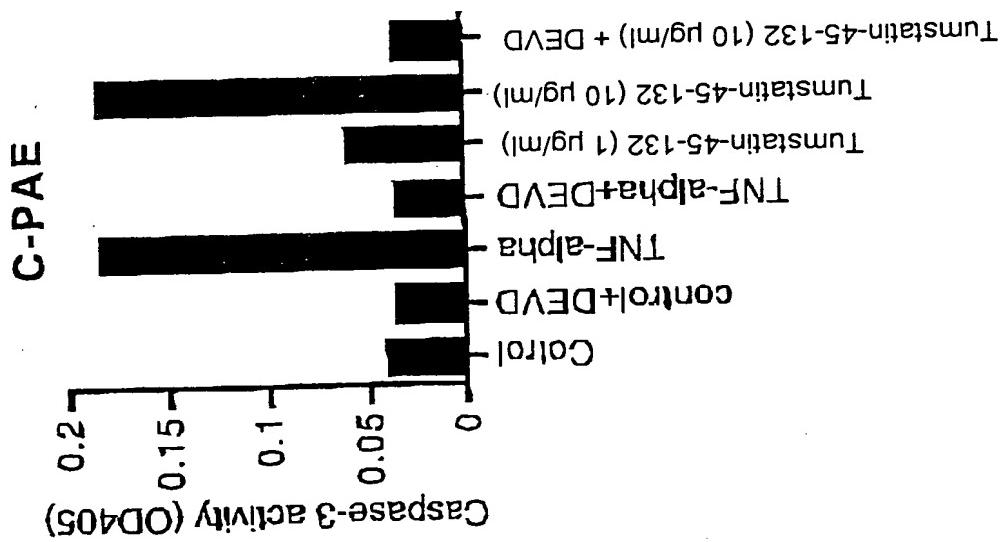
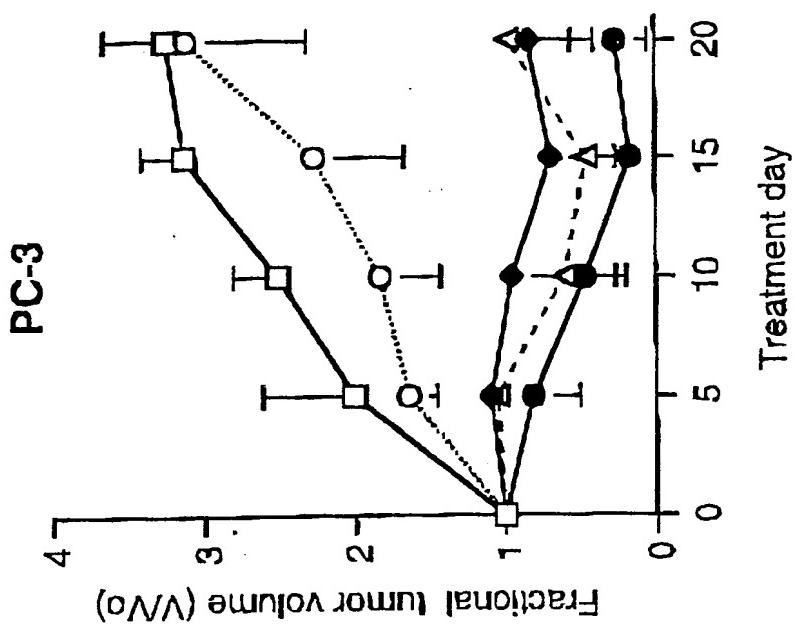


Fig. 53  
Fig. 54



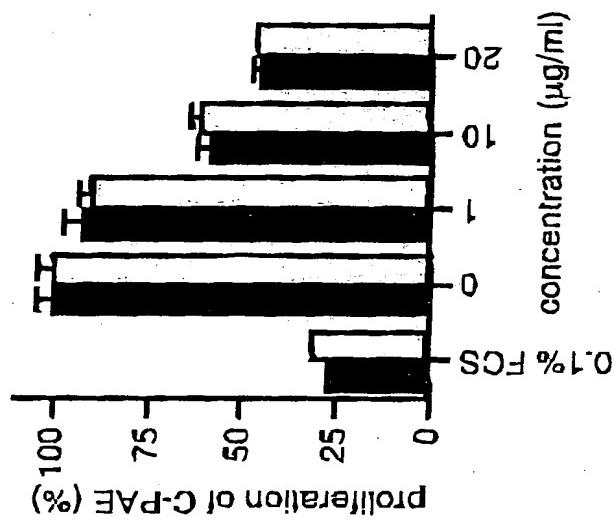


Fig.  
56

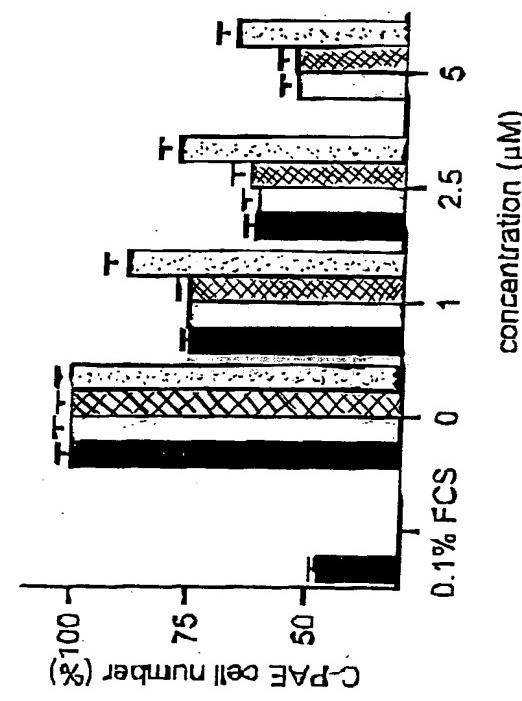


Fig.  
57

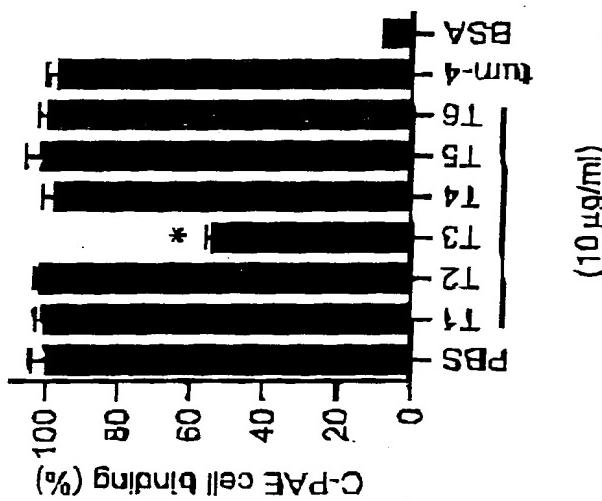


Fig.  
55A

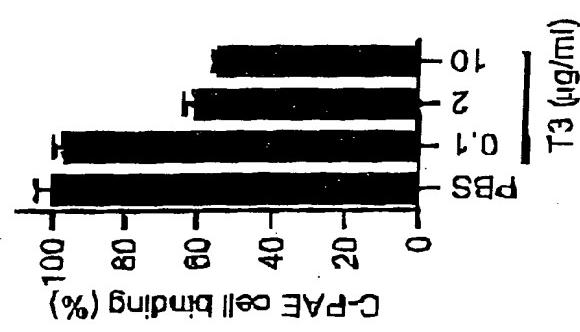


Fig.  
55B

Fig. 58A

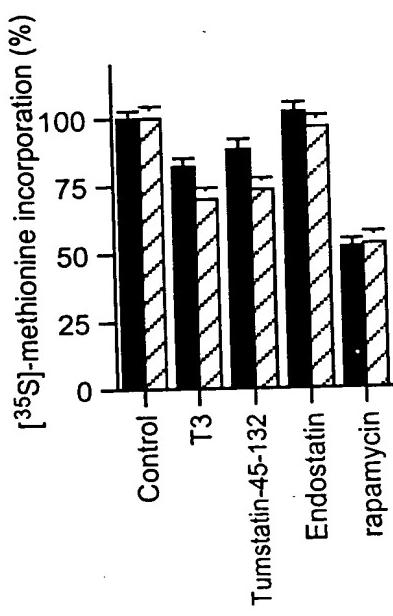


Fig. 58B

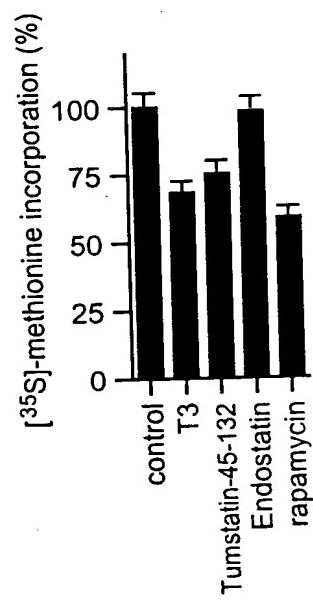


Fig. 58C

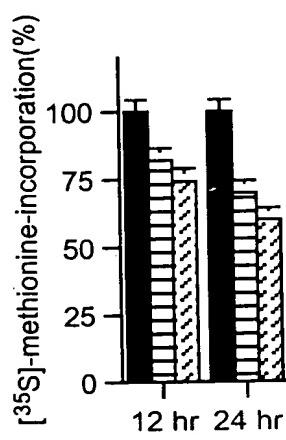


Fig. 58D

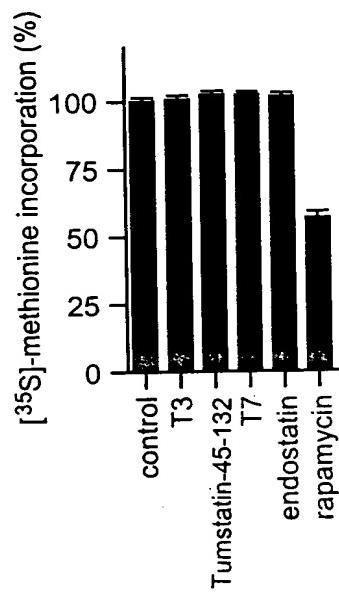


Fig. 58E

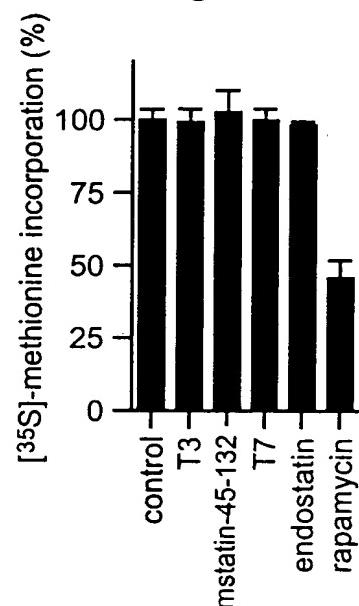


Fig. 58F

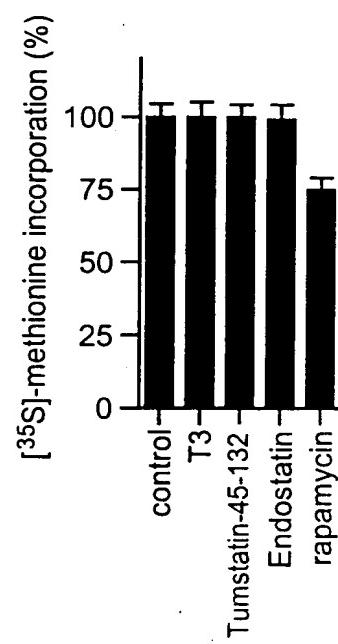


Fig. 58G

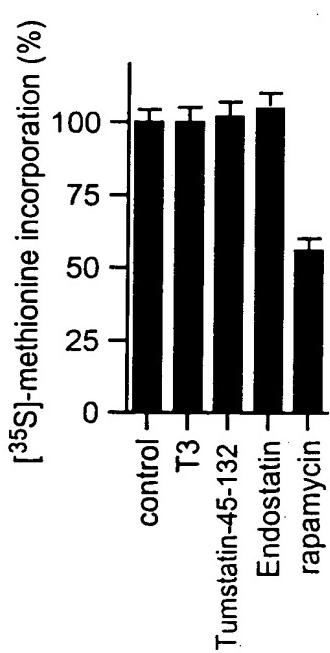


Fig. 58H

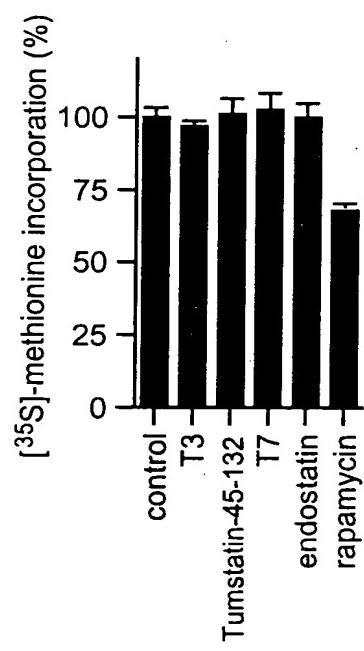


Fig. 59A

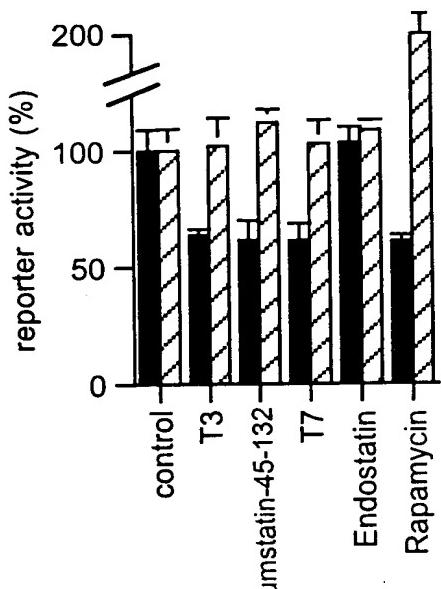


Fig. 59B

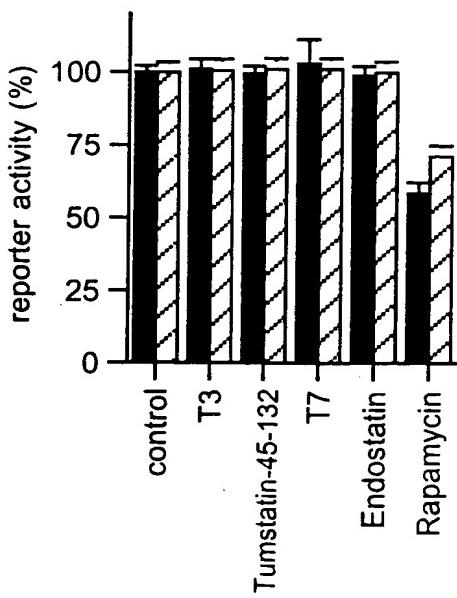


Fig. 60A

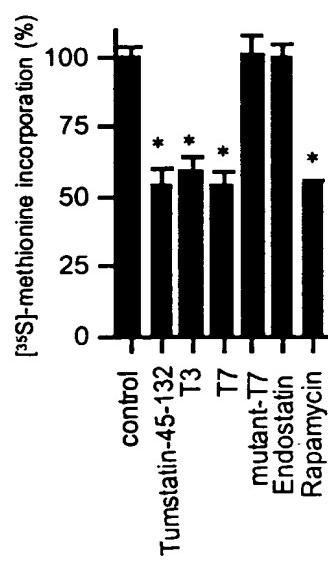


Fig. 60B

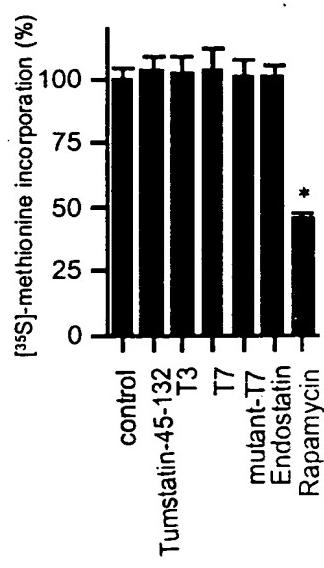


Fig. 60C

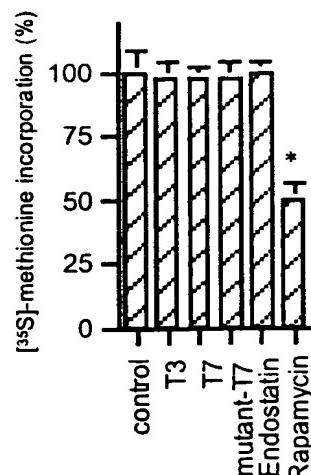


Fig. 60D

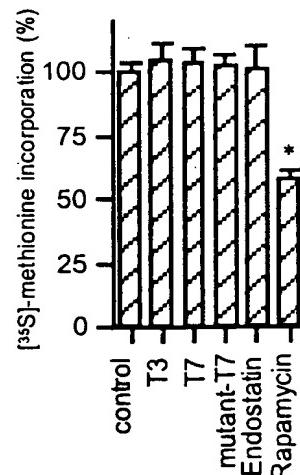


Fig. 60E

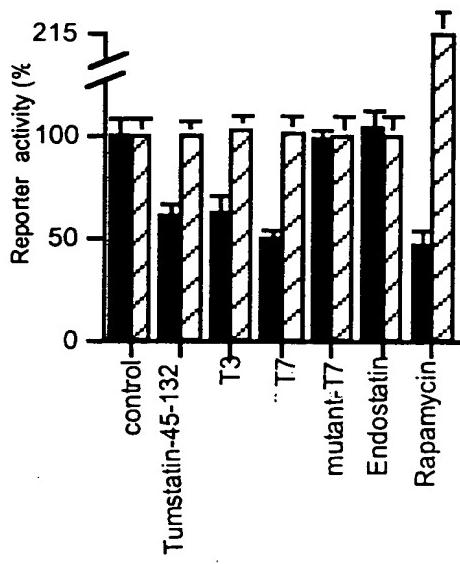


Fig. 60F

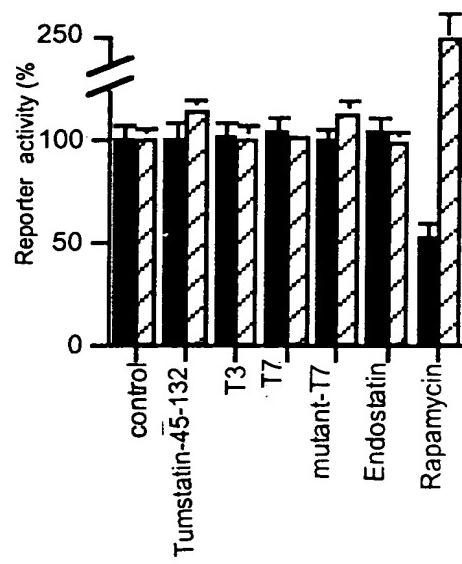


Fig. 60G

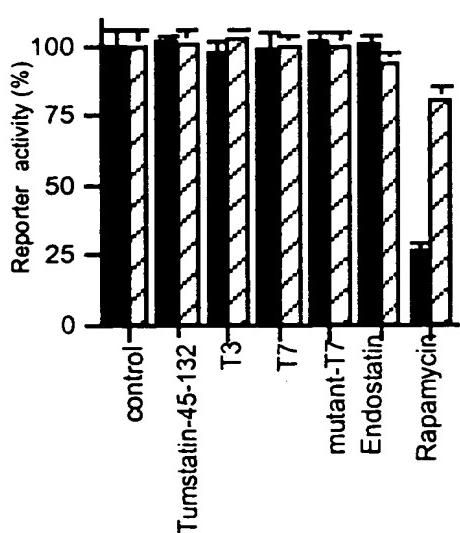


Fig. 60H

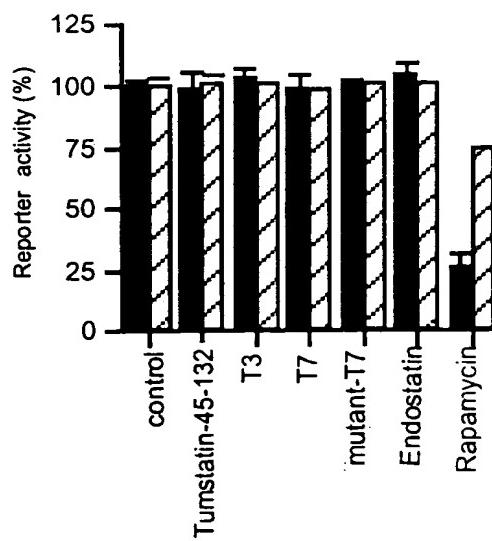


Fig. 61A

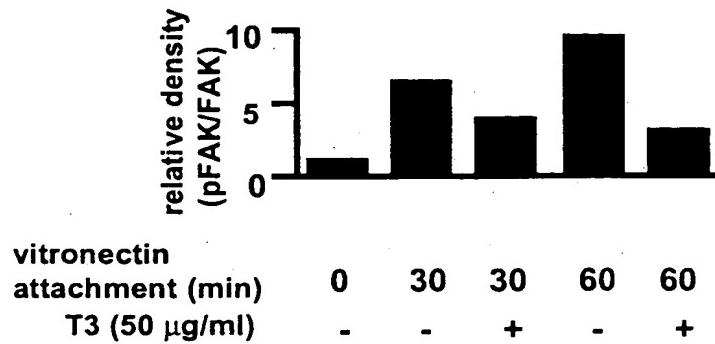


Fig. 61B

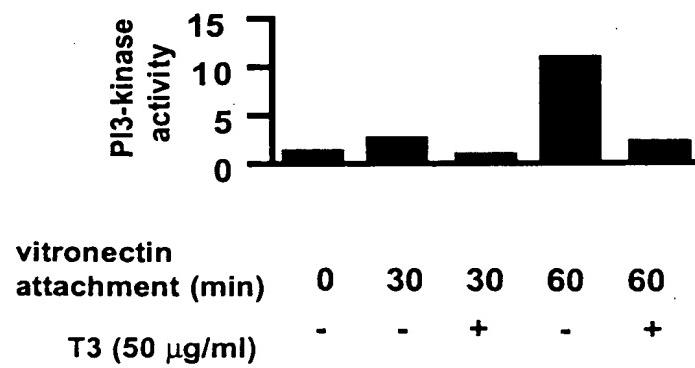


Fig. 61C

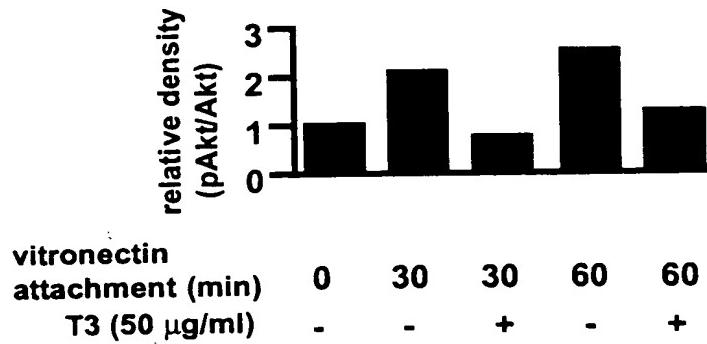


Fig. 61D

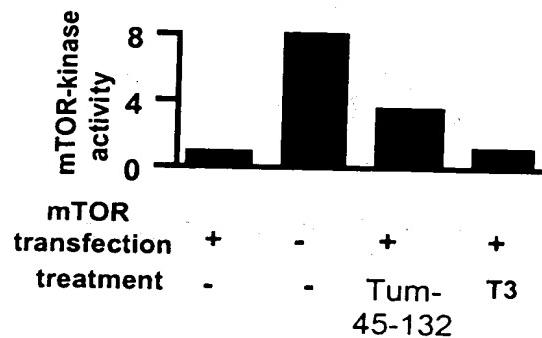


Fig. 61E

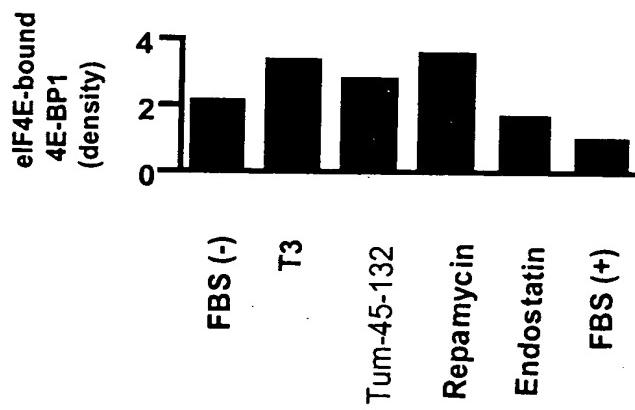
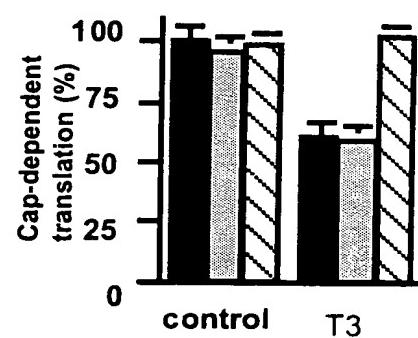


Fig. 61F



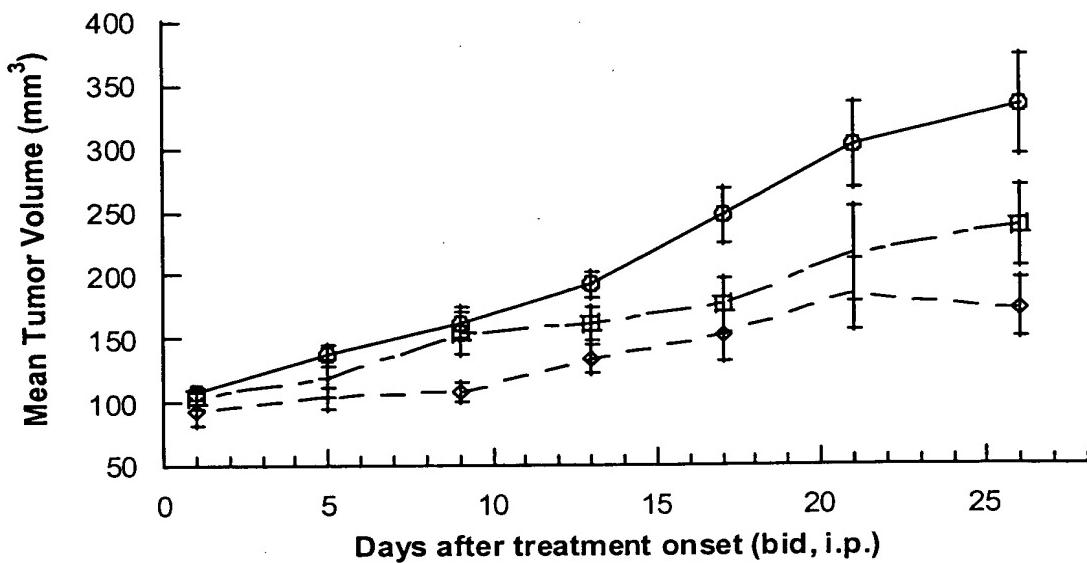


Fig. 62

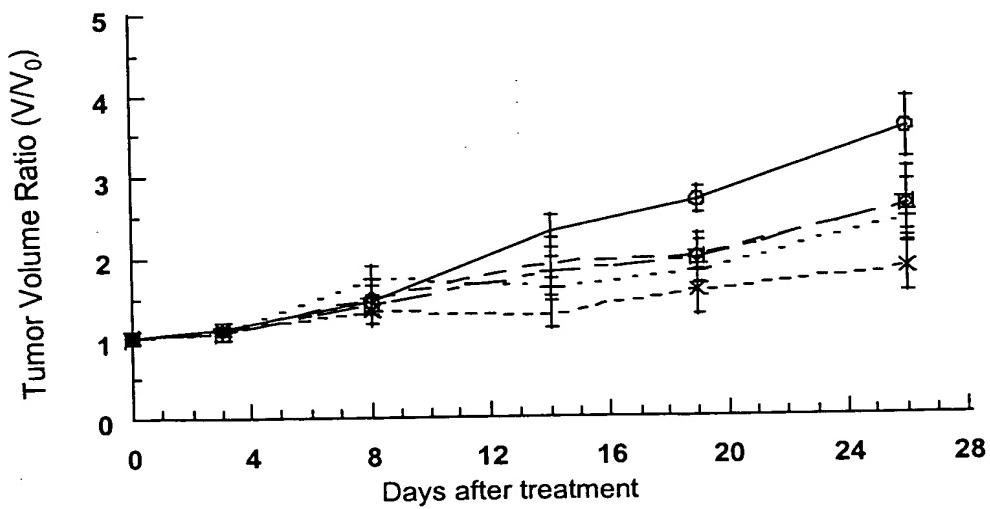


Fig. 63

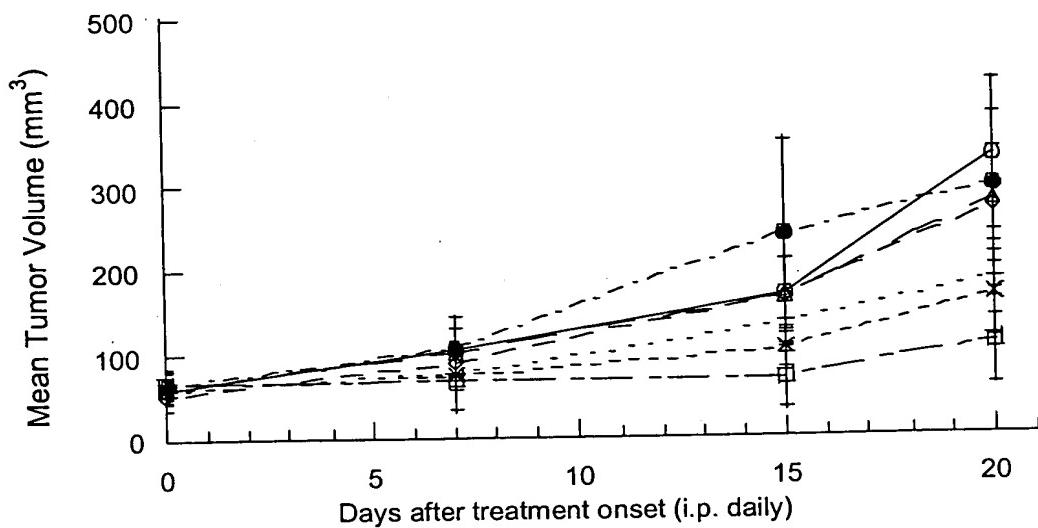


Fig. 64A

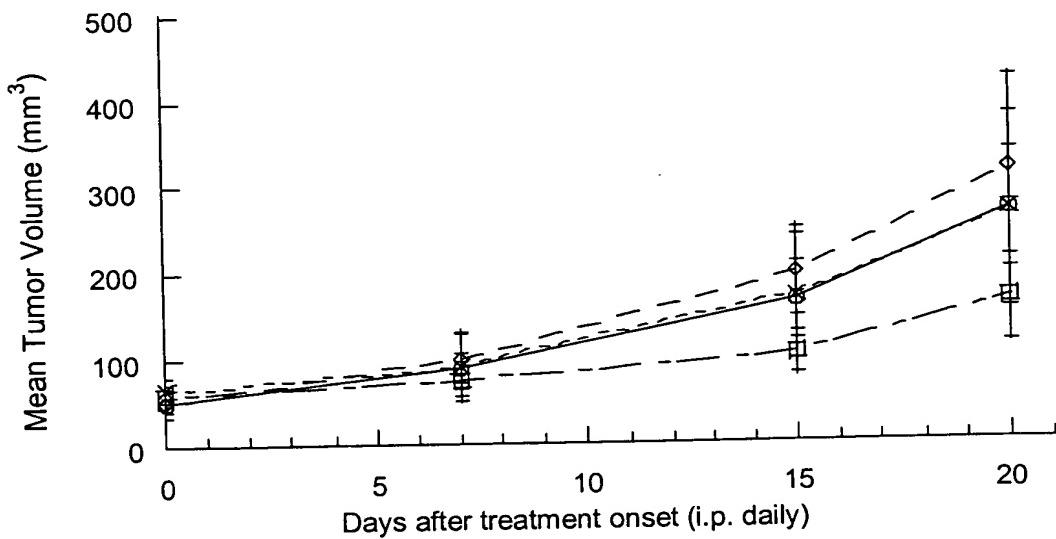


Fig. 64B

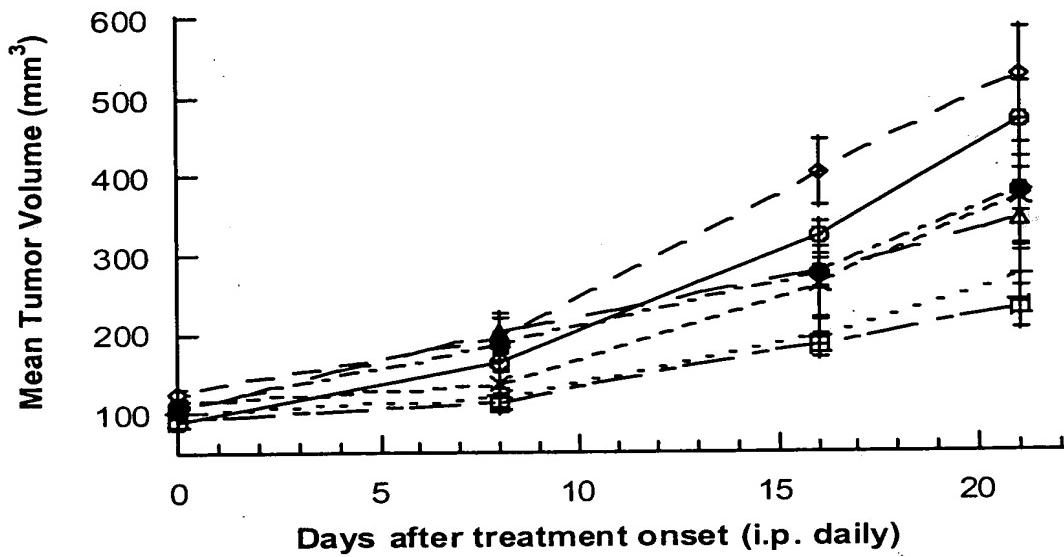


Fig. 65A

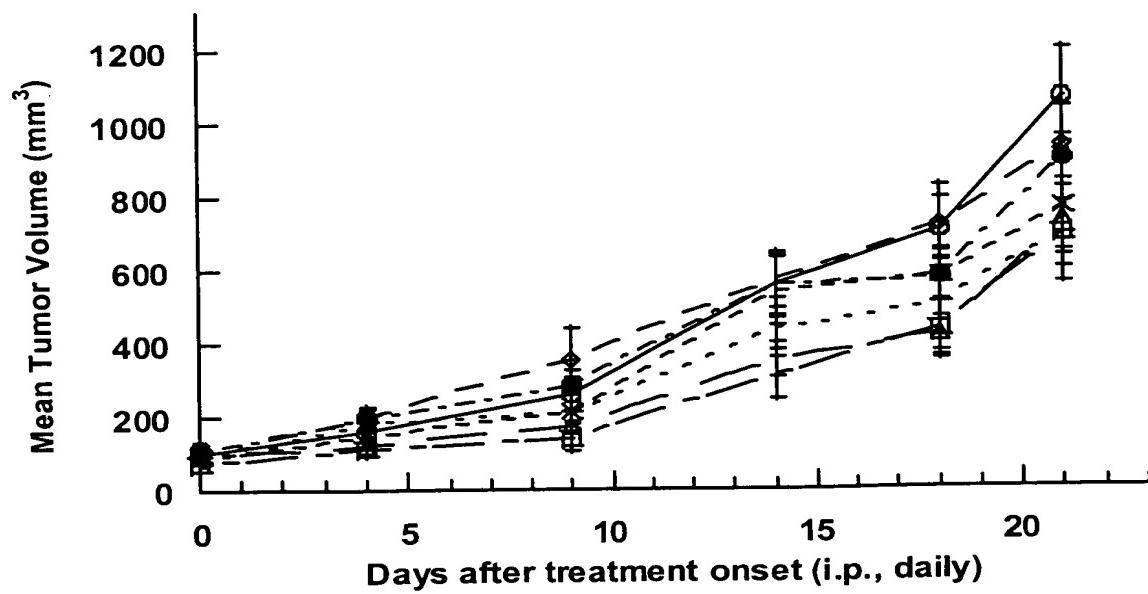


Fig. 65B